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I.

THE SURGICAL REPAIR OF FACIAL NERVE PARALYSES: A CLINICAL PRESENTATION.*

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NEW YORK.

It is now nearly six years since Sir Charles Ballance and I began to work together on the operative treatment of facial palsy. That I ever became deeply interested in it is only because of his outstanding prominence in the development of the surgery of the facial nerve, from the time of its inception, and his intriguing invitation to me to join him in further research.

You are familiar with the animal experiments carried out at my country place. After a year these experiments led up to the Ballance-Duel operation which we have since used on humans. You know also the continued work on animals by which a year later I brought out the employment of the degenerated anterior femoral cutaneous nerve for repair material. We believe that this hastens the time and probably improves the quality of the direct line repair of the facial nerve. It is now well established that this direct line repair is quite superior to the anastomosis of any of the adjacent motor nerves in the neck for the repair of facial nerve palsy.

A clinic for the treatment of facial palsy has been established at the Manhattan Eye, Ear and Throat Hospital, to which all such cases are now referred. This has the advantage of concentrating

*Read before the Section of Otolaryngology, New York Academy of Medicine, April 17, 1935.

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experience on a new and difficult type of surgery, and will eventually result in its improvement, just as concentration on major laryngeal surgery and bronchoscopy has brought about tremendous advances in the technic of that difficult work. I do not mean that other clinics in New York or other centers should not undertake the work. I believe, however, that those who do attempt the work should so prepare themselves, by experience on the cadaver, that they would have a preconceived plan in their mind as to what is to be done in any particular case. Changes in technic which may improve any method may be conceived as a result of experience. In my opinion, such changes should be practiced on the cadaver "propter hoc," and not "post hoc."

The surgery of the facial nerve is most fascinating and most difficult. It can only be learned by cadaver experience; and neither "by the light of heaven," as Ballance often said, nor by reading brochures. The work will repay any of you who wish to approach it from this point of view, not, I can assure you, by any pecuniary rewards, but in the satisfaction in achieving brilliant results in otherwise hopeless cases.

Dr. Tickle and I had the opportunity of seeing well over 100 cases of facial palsy. We have selected and operated on 87 of this number. I have operated on 77; Dr. Tickle has operated on 10.[1]

The operative technic has been developed by frequent returns to the morgue to work out an idea which was verified or abandoned by trial on the cadaver.

I only mention this to fortify the suggestion that all who undertake the operation have a preconceived notion of what they propose to do with that particular case. Dr. Tickle will tell you our present method.

I am showing you seventeen cases to demonstrate results in a cross-section of the most varying types of cases, ranging from the early cases, where the undegenerated graft was employed, up to the present, where only degenerated grafts are used.

While these cases show what seems to me brilliant results as compared with other methods of surgery of the facial nerve, let me hasten to say that no case of repair of the facial nerve can ever be perfect. Although there may be emotional as well as voluntary con-

1. At the time of this correction the number of operated cases has now mounted to 120.

trol, and although movements may be synchronous with the other side, the best repair that will ever be made will never equal the normal side.

We have now learned, as we have demonstrated on some of our patients, that education of the defective side, by voluntary control through the neokinetic nervous system, may improve facial expression tremendously. The reason for this imperfection in the repaired side is due not so much to a lack of restoration of as much vigor to the recovered muscle, as it is to the fact that split neurons, wandering to the wrong destination, produce on stimulation an assymetry of response in the facial muscles. In our early enthusiasm over results in the direct line repair, we spoke of the absence of associated movements such as those which occurred in the repair by anastamosis of the facial with the adjacent motor nerves in the neck. We now appreciate that there are no facial movements which are not association movements in the sense that different groups of muscles enter into the final expression; and that, due to the mix-up of peripheral distribution in the axons of a repaired nerve, the restored muscles can never quite equal the normal side. This is not so much a criticism of the results which you have seen as it is a recognition and explanation of necessary defects, which are often apparent.

As experience grows the wonder in my mind is not so much at the defects which one observes as that they are not much more conspicuous. If the repair of a peripheral nerve for the restoration of muscles in the arm, or leg, or hand, were made, education would bring about an appearance of perfection in the result which can hardly be expected in the nuances of synchronous facial expression.

We have elsewhere on repeated occasions spoken of the types of accidental cases and our attitude towards their operative treatment. Dr. Tickle will tell you more of our present ideas on this subject.

I should like now, in addition, to call your attention to a somewhat more clarified attitude toward cases of so-called "Bell's palsy." As you know, these cases are produced by a toxic invasion of the nerve which causes a squeeze on the neurons within the fallopian canal. Without too much accuracy, let us assume that 80 per cent of such cases recover in four to six weeks, exhibiting no noticeable defect in movements of the face. Let us assume that the remaining 20 per cent have a much more violent invasion, and that a partial recovery takes place after long periods of three, six or twelve months. Experience has led me to a theory that in the milder cases the inflam-

matory squeeze on the neurons is so slight that complete Wallerian degeneration in the distal segment does not take place. The face is paralyzed temporarily, but the Faradic response never entirely disappears. Such cases recover perfectly. The remaining 20 per cent I believe lose their Faradic response in two or three days, from the violent inflammatory squeeze within the tubes. The condition is analogous to that encountered in the cases where the nerve is severed or severely injured. I believe that if we recognized that such cases would never entirely recover if left alone, that we would do an early decompression, thereby insuring as nearly a perfect recovery as we get in the acute cases of injury.

I show you two or three cases to illustrate what I mean by this rather bold position. Case 14, a nurse at the Manhattan Eye, Ear and Throat Hospital, came to us on August 15, 1933, with a complete palsy of her left side. We saw her daily, and, under the pretext of electrical treatment, verified that she never lost her Faradic response in the muscles, although there were no voluntary movements for two or three weeks. She recovered perfectly, however, in about four weeks. This is a typical case of the 80 per cent group of mild invasion with perfect recovery without treatment.

Case No. 15 came to the office on June 30, 1934, with a history of two years previously having an attack of facial palsy similar to Case No. 1. Two years later a recurrence on the same side was followed by a palsy which had persisted when we first saw her for about nine weeks. There was still a complete reaction of degeneration, a complete loss of response to Faradic current, and exaggerated response to the galvanic positive closure. Realizing the difference in time of recovery from her previous experience, she was anxious to have something done for her relief. The nerve was decompressed by removal of the bony fallopian canal up to the level of the horizontal semicircular canal, and the sheath split from this point to the level of its opening at the stylomastoid foramen. The wound was closed; (a week later), Faradic response began to appear in the face. A month later her recovery was as perfect as you see it.

The captions on No. 16 and No. 17 are self-explanatory.

135 East 64th Street.

THE AFTER-CARE OF SURGICAL REPAIR OF THE FACIAL NERVE.*

THOMAS G. TICKLE, M.D.,

NEW YORK.

The successful recovery in operations performed for facial palsy due either to accidental injury or a so-called "Bell's palsy," from toxic invasion, depends not only on the technic of the operation but also quite as much on the after-treatment.

We have found in either type of operation that it is very important in the preparation of the operative field to make certain that the external auditory canal, above all, has been thoroughly sterilized.

We have observed that a number of our cases, in which we apparently had been most careful of our technic have, four or five days later, shown infection in the wound.

At first we attributed this either to some faulty preparation of the field of operation, or to the use of dressings which were not absolutely sterile, or perhaps to both. After much discussion, we determined to try the following plan in the hope that we might overcome this difficulty. The external auditory canal is filled with 3 per cent tincture of iodine. This is allowed to remain for five minutes, and is then sucked out by means of a medicine dropper, and replaced by one or two instillations of 95 per cent alcohol within the next few minutes. The alcohol is employed, first, to remove all the iodine, since, as you all know, the presence of antiseptics may be unfavorable to the union of the graft; and, second, to guard against the severe dermatitis which sometimes happens where iodine is used in the presence of moisture, and the partial exclusion of air by dressings. The canal is finally washed out thoroughly with normal saline solution.

This plan of preparation is adopted in all operations of the facial nerve. Since we have used it we have had no suppuration following operation in the clean cases. In other words, meticulous sterilization of the canal is the most important part of the preparation of the operative field.

*Read before the Section of Otolaryngology, New York Academy of Medicine, April 17, 1935.

There are two types of cases which we are called upon to operate: First, those due to accidental injury of the facial nerve in operations on the mastoid; and second, those in which toxic infection or refrigeration of the facial nerve have produced a facial palsy. Such cases may be of long standing with a partial recovery of facial movements, or of comparatively short standing with a complete palsy.

We have quite definitely decided that the accidental cases should be preferably explored at once. If an injury of the facial nerve has caused the paralysis of the facial muscles an immediate investigation has the advantage that the segment of the facial nerve distal to the injury retains response to Faradic stimulation for from forty-eight to seventy-two hours. No matter where the injury is, the advantage of being able to identify the distal segment by Faradic stimulation is of great advantage. Any exploration subsequent to this short period can only be by an anatomic dissection. In the acute cases, if the injury has been found to be an actual destruction of the neurons over any length, a preliminary preparation of the femoral cutaneous nerve, for subsequent repair material, can be made at this time. Two or three weeks later the gap is repaired by a graft taken from this degenerated nerve.

If, however, the injury is found to be only to the sheath, a decompression of the nerve, which includes slitting of the sheath above and below the site of injury, will be all that is necessary for the subsequent repair of the nerve.

The other types of cases are those in which the Faradic response has been absent for days, months or years. In these cases the anatomic dissection of the nerve over the point of injury must be done, without the aid of Faradic response in the distal segment.

We have concluded that in all cases it is better to expose the nerve from the stylomastoid foramen up to and proximally beyond the injury. Even in the cases which are to be decompressed only the outer half of the bony tube distal to the injury should be removed, all the way from the stylomastoid foramen up. Finding the nerve at its exit from the foramen and removing the bony covering upward, we have found to hazard the minimum chance of injury during the dissection. In decompression of the nerve for Bell's palsy we now close the wound immediately after splitting the sheath of the nerve without covering the slit by dentist's gold foil. Whenever the wound is left open, gold foil is placed over the slit. The flaps are protected with perforated rubber tissue. This prevents the gauze dressings from adhering and causing troublesome bleeding on their removal. It

also has the advantage of rendering the dressings comparatively painless. All wounds that are left open are lightly packed with sterile gauze wicks about three inches long wrung out of normal salt solution. No antiseptics or hemostatics or local anesthetics are used. It is important to stop hemorrhage just at the time of the insertion of the graft to prevent a blood clot between the opposed ends. The ooze from the bone is best stopped by the use of saline solution, about 120 degrees Fahrenheit, and patient waiting. During the earlier cases this was persisted in until all bleeding was stopped and entailed the loss of much time. We have now discovered that if the ooze of blood can be stopped temporarily so that the ends of the graft may be closely opposed to the proximal and distal segments that the subsequent ooze, far from being detrimental, is really beneficial, since it helps to fix the graft in position in a fibrinous clot which subsequently organizes.

The dressings are now changed daily in the cases which are badly suppurating; in the others, at intervals of two to four days. At the time of changing the dressings the suppurating wounds are cleansed with salt solution only by numerous instillations and withdrawals by means of a medicine dropper.

The final plastic closure of the wound must depend on judgment in each individual case. Where the wound is sufficiently filled in with healthy granulations plastic closure may be done at any time. Since we have used degenerated grafts, we have found it of some advantage to postpone the plastic closure for at least a month. At this time we have on several cases been able to elicit a Faradic response by use of a current so strong that it would have been unbearable without anesthesia. This early response may occur weeks before any voluntary movements take place. It is a great comfort, since it always is the harbinger of a successful outcome of the case.

A word regarding the subsequent treatment of operative cases by electric stimulation. The Faradic current acts only through the neurons of the facial nerve. Response to it, therefore, indicates that there is a connection from the central nucleus to the muscle. Response to the galvanic current takes place in muscle fiber over long periods following the complete loss of response to Faradic stimulation. You all know the classical reaction of degeneration phenomena. We believe that Faradic stimulation is useless except for purposes of diagnosis and do not employ it in recovering cases or in cases of partial paralysis. We think that the use of galvanic electricity, the interrupted anodal closure over the muscles of the face, for a few min-

utes once or twice weekly, before and after operation, is beneficial in keeping up the tone of the muscle. We do not advise operation in cases where there is no response in the muscle to galvanic stimulation. In all our cases we continue galvanic stimulation until facial movements have reached their maximum improvement. The intervals must be a matter of judgment. It is possible to overdo it. In practice it is a great help, since the patient may be kept under observation, returning for regular treatment, because they believe the continued improvement is the result of electricity. We feel that we keep the clinic patients under long observation by this method.

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Case 1—Fig. 1

Case 1—Fig. 2.

Case 1—Fig. 3

Case 1—Fig. 4.

CASE No. 1.

Baby G., 8½ months.

26 mm. freshly incised graft from anterior respiratory nerve of Bell.

Paralysis had existed only two days. This case shows the advantage of early exploration, since Faradic response is still present in distal segment for 72 hours.

Suppurating wound.

Nearly perfect emotional responses due to slight development neokinetic control in this very young patient.

First Faradic response in 90 days.

It is now four years and one month since the operation.

We learned from this first case in which a fresh graft was employed that suppuration in the wound is not a bar to success. A clean wound, though preferable, is not essential to success.

In more than 100 operated cases, we have now employed grafts successfully in suppurating wounds, in 20 cases.

Case 2—Fig. 1.

Case 2—Fig. 2.

CASE No. 2.

Mrs. B., 34 years old.

30 mm. freshly incised from graft Bell's anterior respiratory nerve.

Operation 11 months after original injury.

No Faradic response in facial muscles.

Good Galvanic response.

Suppurating wound.

First Faradic response in 180 days.

It is now three years and ten months since the operation.

We learned from this case that length of time following the accident, length of graft, a suppurating wound, do not bar success. Any length of gap, any condition of infection may be overcome. The one essential is that there should be an active response to Galvanic stimulation in the muscles of the face.

Case 3—Fig. 1.

Case 3—Fig. 2.

Case 3—Fig. 3.

CASE No. 3.

C. C., seven months after injury.

In this case we changed to the intercostal nerve, because we found that the large dehiscences required the use of so much of the nerve of Bell that it was impossible to reunite the severed ends, as we had done in animals where shorter grafts were used. As a consequence the innervation of the serratus magnus was ruined. We sought a motor nerve whose loss of function would be of less consequence.

Case 4—Fig. 1

Case 4—Fig. 2.

Case 4—Fig. 3.

CASE No. 4.

W. S.

One month paralysis.

Good Galvanic response.

No Faradic response.

12 mm. freshly incised, double strand, intercostal nerve.

It is now three years and one month since the operation.

In this case a second strand was used. We now frequently use two strands, occasionally three, where the graft material is smaller than the facial. We believe that two or three smaller strands are more efficacious than one large one.

Case 5—Fig. 1. In action before operation.

Case 5—Fig. 2. In repose 10 months after operation.

Case 5—Fig. 3. In action 10 months after operation.

It is now 2 years and 5 months after operation.

CASE No. 5.

A. J., 15 years.

Graft 12 mm. degenerated anterior femoral cutaneous nerve.

The degenerated graft had been successfully employed in animals in several cases.

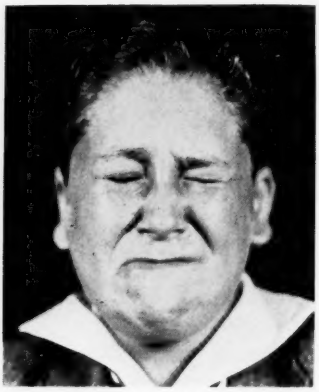
This was the first case in which a prepared nerve was employed in humans.

Faradic response in facial muscles appeared in 30 days.

Case 6—Fig. 1. Before operation, in repose.

Case 6—Fig. 2. In action.

Case 6—Fig. 3. Two and one-half years after operation, in repose.



Case 6—Fig. 4. In action.

CASE No. 6.

J. W.

Graft transplanted one month after injury.

16 mm. prepared anterior femoral cutaneous nerve.

Case 7—Fig. 1.

Case 7—Fig. 2.

Case 7—Fig. 3.

CASE No. 7.

F. A. Femoral cutaneous degenerated graft 10 mm. implanted three weeks after injury.

Case 8—Fig. 1

Case 8—Fig. 2

Case 8—Fig. 3.

Case 8—Fig. 4.

CASE No. 8.

A. L. Eleven months after injury.
Transplant of 38 mm. degenerated anterior femoral cutaneous nerve.
Long period of complete palsy.
Very long graft. Suppurating wound.
First Faradic response in five months.
First voluntary and emotional response in eight months.
He is shown in picture overdoing voluntary movement of the operated side.
By education he now has controlled, even, synchronous movements.
Emotional responses are still uneven.

Case 9—Fig. 1.

Case 9—Fig. 2.

Case 9—Fig. 3.

Case 9—Fig. 4.

CASE No. 9.

Mr. S. This case, operated by Dr. Tickle, is interesting because a necrosis of the labyrinth had resulted in a sequestrum the removal of which had included the chochlea, vestibular apparatus, the geniculate ganglion. The facial nerve had formed a neuroma just outside the dura. The plate of bone was removed, the neuroma excised, and a double strand laid from the stump down to the distal segment 16 mm. in length.

The pictures show him, No. 1, in repose, and No. 2, in action before operation.

The wound was infected.

First Faradic response in seven months. First voluntary and emotional response in nine months.

No. 3, in repose 16 months after operation.

No. 4, in action 16 months after operation.

We have been encouraged from this to attempt direct restoration of the "line" in paralysis from fracture of the bone; a class of cases which had been hitherto relegated to anastamosis with adjacent nerves in the neck.

Case 10—Fig. 1.

Case 10—Fig. 2.

Case 10—Fig. 3.

Case 10—Fig. 4.

CASE No. 10.

Mary A., three years old.

Complete palsy following injury in acute mastoid operation. Showing the advantage of immediate investigation. A spicule of bone was compressing the nerve. Uncovering and splitting of the inflamed sheath resulted in a practically complete recovery.

Leaving it alone would have resulted in a partial recovery with grotesque disfiguration for life.

Case 11—Fig. 1.

Case 11—Fig. 2.

Case 11—Fig. 3.

CASE No. 11.

M. Y.

Removal of a cervical gland. Arterial bleeding finally controlled by deep suture passed on a curved needle deep in the wound. The facial nerve was included in the ligature. Result: Complete left facial palsy. Investigation two weeks later.

7 mm. of necrotic facial nerve between stylomastoid foramen removed and replaced by a double strand of freshly excised intercostal nerve.

Case 12—Fig. 1.

Case 12—Fig. 2.

Case 12—Fig. 3.

Case 12—Fig. 4.

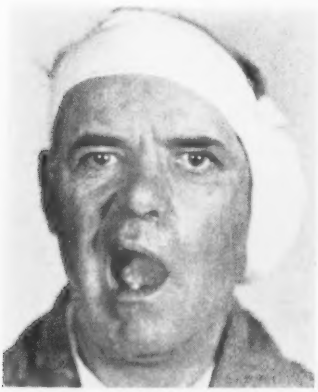
CASE No. 12.

A. P., 26 years old.

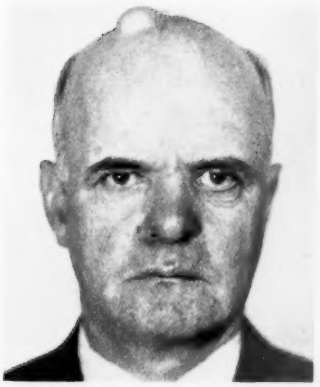
.22 calibre bullet from revolver entered upper lip and lodged behind angle of jaw on left side.

An attempt to remove bullet was unsuccessful but did sever the main trunk of the facial nerve just outside the stylomastoid foramen.

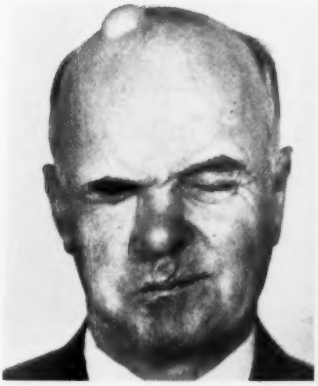
Two months later the facial was reunited with eventual perfect recovery.



Case 13—Fig. 1.



Case 13—Fig. 2.



Case 13—Fig. 3.

CASE No. 13.

J. F.

Eleven days after injury.

Double strand 7 mm. anterior femoral cutaneous nerve degenerated in another individual. Graft material was used for this and another case in addition to the original donor. Both homoplastic grafts (7 mm. and 15 mm.) made excellent recoveries.

Homoplastic grafts (removed from another individual of the same blood type) have been employed in six cases. They have all been successful.

This may have a wide influence in peripheral neural surgery in war injuries.

Case 14—Fig. 1.

Case 14—Fig. 2.

CASE No. 14.

M. M.

Typical case mild Bell's palsy. Faradic response never entirely lost although complete facial palsy was present for about three weeks.

Complete recovery in four or five weeks.

Case 15—Fig. 1.

Case 15—Fig. 2.

Case 15—Fig. 3.

CASE No. 15.

M. D.

An attack two years ago with onset and recovery as in case No. 14. Now has recurrence with a complete palsy which has persisted without improvement for 12 weeks. Typical reaction of Wallerian degeneration.

Decompression of nerve from stylomastoid foramen to the level of horizontal semi-circular canal.

One week later Faradic response appeared in facial muscles.

One month later complete recovery.

Case 16—Fig. 1.

Case 16—Fig. 2.

Case 16—Fig. 3.

CASE No. 16.

N. S.

Double Bell's Palsy.

Left side 10 years—partial recovery: recent recurrence with complete palsy.

Right side—six months with partial recovery.

Double decompression.

Even synchronous movements of both sides.

Patient rescued from practically social ostracism.

Case 17—Fig. 1.

Case 17—Fig. 2.

Case 17—Fig. 3.

CASE No. 17.

Mrs. C.

Two years after partial recovery from Bell's Palsy.

No. 1 in repose.

A decompression was done from the stylomastoid foramen to the level of the horizontal semi-circular canal. The sheath was slit open. A few strands were found to be running through. These were not disturbed. A piece of degenerated anterior femoral cutaneous nerve was implanted from the level of the horizontal semi-circular canal down to the trunk of the nerve outside the stylomastoid foramen. This lay upon the attenuated portion of the nerve caused by the compression by the inflammatory squeeze of the Bell's palsy. The patient never lost the partial movements of the face, but in a few months showed the remarkable improvement from additional axons running through the graft.

No. 1 and No. 2, four months after reinforcing graft.

II.

RESECTION OF THE ENTIRE THORACIC ESOPHAGUS FOR CARCINOMA.*

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NEWARK.

It was in 1925 that I first, with the assistance of the thoracic surgeon, attempted to remove the esophagus in a patient, age 57, who had complained of the inability to swallow solid food of one month's duration. X-rays showed a stricture of the esophagus in the lower third. Esophagoscopy gave us a picture at 33 cm. from the teeth of a small mass bleeding readily on contact. A specimen was removed for biopsy, the report of which was squamous epithelioma.

The general physical condition of the patient was of such a good risk that I suggested to him the advisability of operation by the posterior route. He readily consented. The thoracic approach to the growth was done by Dr. Dieffenbach. We found that the growth at this time had extended so far around the esophagus that it was impossible to separate it from the surrounding tissue. The thorax was closed and a gastrostomy was done.

It was so discouraging to me that I made no further attempts to remove the esophagus in any patients until 1934, when, after reading Professor Grey Turner's article in the *Journal of Laryngology and Otology* in May, 1934, I received a new stimulus to try his procedure. Fielding O. Lewis' attempt to remove the upper third of the esophagus, reported before this Society in 1934, encouraged me still further. My first patient lived sixteen days following complete removal of his esophagus. The second patient died of a mediastinitis thirty-six hours after operation. The following are the case reports:

REPORT OF CASES.

CASE 1.—M. M., harnessmaker, age 71 years, male, white, weight 167 pounds, was admitted to the Bronchoscopic Clinic at the Presbyterian Hospital, May 25, 1934, complaining of a sensation that his throat was closing when swallowing.

*Read before the eighteenth annual meeting of the American Bronchoscopic Society, Toronto, June 1, 1935.

No history of cancer in family. Wassermann and Kahn were negative. X-ray examination of the esophagus by means of barium meal showed marked narrowing about the middle of the esophagus. There was no definite evidence of a diverticulum, and yet the filling defect was not typical of cancer.

June 28, 1934, esophagoscopy was done and a biopsy was taken from a small bleeding area 31 cm. from the teeth. The report of biopsy showed necrosis with polymorphonuclear and eosinophilic infiltration. There was an overgrowth of stratified squamous epithelium in nests invading the submucous tissue, few mitotic figures and some cornification. Ulcerated epidermoid carcinoma, Grade II malignancy. The urine was negative, and the blood chemistry normal.

July 14, 1934, under avertin-ether anesthesia, incision was made in the abdomen, midline, from the ensiform cartilage downward; the stomach was exposed. The left lobe of the liver was detached from the diaphragm and pushed out of the field of operation. The abdominal esophagus was isolated. The peritoneal coat covering the esophagus was incised and then by blunt finger dissection the esophagus was freed from its areolar tissue through the diaphragm and thorax as far as the finger could reach. I then made a longitudinal incision in the neck from the

Fig. 1. Picture of esophagus that was removed.

midline just above the clavicle to the posterior border of the sterno-cleido-mastoid muscle on the left side. The sterno-cleido-mastoid muscle was cut through at the clavicle and with careful dissection the esophagus was isolated, then with finger dissection the esophagus freed from the trachea downward into the mediastinum. At the same time, Dr. Dieffenbach working from below through the abdominal wound, the esophagus was completely freed from its attachments. At the level of the clavicle the esophagus was ligated and severed; a clamp put on the proximal end and this was brought out of the neck and sutured to the skin. A temporary pack was placed in the superior mediastinum. Dr. Dieffenbach then by gentle traction removed the thoracic esophagus by way of the abdomen. About 2 inches from the stomach the esophagus was severed by means of cautery and this was used as an opening for a gastrostomy. Time of operation, two hours and fifteen minutes.

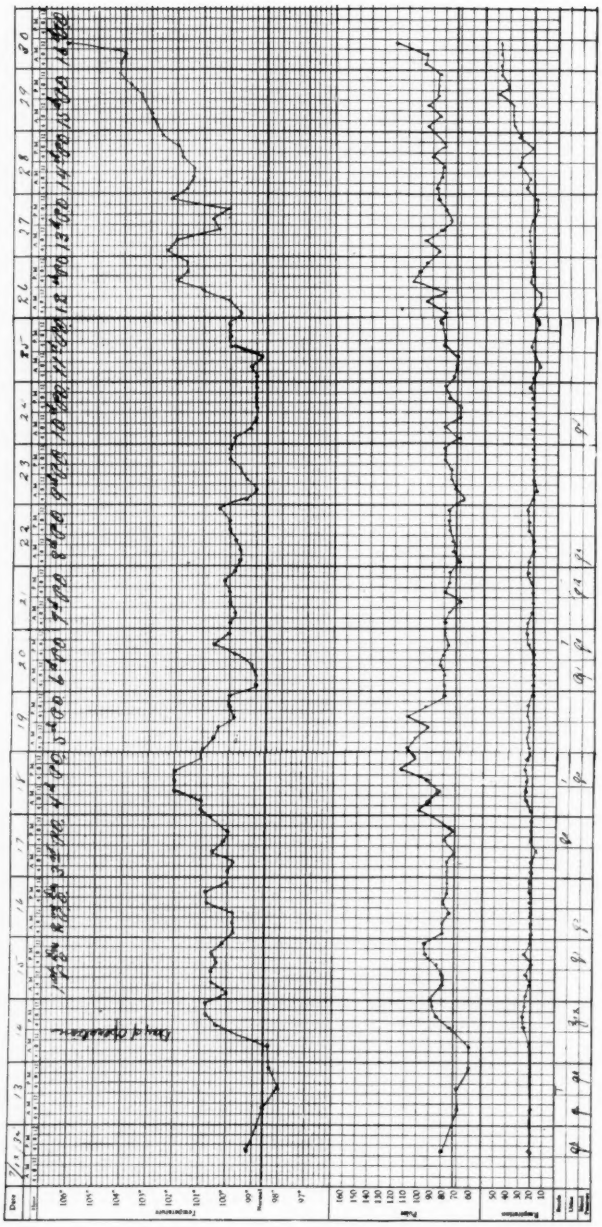

Fig. 2.

The night following the operation the patient got out of bed and walked tc the bathroom; was not delirious; said he did not wish to trouble the nurse; he did the same thing the following day. What bearing this had on his abdominal wound is hard to say, but we feel that it did have some effect, for on July 24th it becamt necessary for us to suture the gastrostomy opening to the abdominal wall which had sloughed. This did not prevent leakage. On July 27, Dr. Dieffenbach did an enterostomy but the patient became gradually worse and died on the 30th, sixteen days following the operation.

CASE 2.—M. P. Service of Dr. Sprague. German, age 56 years, white, male. Admitted to Newark City Hospital, January 16, 1935. Occupation, bartender. Came to hospital with provisional diagnosis of malignancy of stomach or esophagus. No hereditary history of cancer. Antecedent personal history: General health had been fair. Used tobacco in form of chewing moderately. Onset: dysphagia of one week's duration. During last month or two patient has not been feeling up to par. Has had considerable anorexia, and in the last four weeks has lost about ten pounds. About five days ago he began to develop dysphagia, inability to swallow solid foods, and regurgitation of food apparently swallowed with a sensation that it had not reached his stomach. Has had tarry stools occasionally during the last two months, the last occurring about four days ago. Physical examination: Fairly well nourished white male, 56 years of age, with history of vomiting for past month. Head, scalp normal. Eyes, pupils react to light and accommodation. Nose and ears negative. Mouth, teeth poor; no nodes in the neck; heart and lungs negative. Abdomen, flaccid, no tenderness; liver and spleen enlarged; extremities normal. Wassermann and Kahn negative.

On January 24th was referred to me for esophagoscopy, which was done, and at 35 cm. from the teeth we saw a mass bleeding readily on contact, from which a specimen was taken for biopsy. The report of the biopsy was an epidermoid carcinoma Grade II.

On January 30th, Dr. Sprague did a gastrostomy, Spirack type. March 1, 1935, we removed the esophagus as described in case 1. The esophagus, however, did not separate as readily, and had many firm adhesions around the left bronchus. We believe that one of these adhesions prevented the easy removal of the esophagus. The pulse, temperature and respiration steadily going up after the operation, patient dying in 43 hours.

CONCLUSIONS.

The entire esophagus may be removed surgically by the pull through method of Turner.

I feel the same as Dr. Mosher, that the so-called liver approach to the lower end of the esophagus is likely to give the best results from surgery.

The one-stage operation, to my mind, seems to be easier.

Early diagnosis is essential for the best operative results.

My thanks to Drs. Dieffenbach and Sprague for their kind assistance in these cases, notwithstanding our failure to effect a cure.

24 COMMERCE STREET.

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III.

AN EXPERIMENTAL ANALYSIS OF THE VESTIBULAR POINTING TEST.*

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Since the introduction of the so-called "pointing test" *(Zeigeversuch)* by Bárány,[1] in 1911, as a clinical index to the functional integrity of the vestibular apparatus and certain associated neural pathways, there has been much discussion regarding its physiological basis and diagnostic significance. The major issue involved in this controvery has been admirably summarized by Watkyn-Thomas and Yates,[27] in their recently published "Principles and Practice of Otology," in the following words:

> "There are two possible explanations of the results [of the pointing test]:
>
> "1. That they are a subconscious correction to compensate for the sensation of vertigo; the subject feels that he is moving to the left, and to touch an unseen object . . . moves the hand . . . to the right.
>
> "2. That they are manifestations of a change in muscle tone of the two sides [of the body] induced by labyrinthine stimulation or depression."

The problem as to which, if either, of these two hypotheses is correct is of more than merely theoretical importance and seemed to the writers to warrant careful investigation.

EXPERIMENT I.

In a publication which appeared in 1882, William James[16] quotes a letter from a physician who claimed that he had "succeeded in abolishing the sense of vertigo" in hypnotized subjects and that they were thus rendered capable of walking normally immediately

*The experiments here reported were carried out in the Psychology Laboratory of the Johns Hopkins University.

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after rapid bodily rotation, a performance which James' correspondent regarded as impossible in nonhypnotized subjects. This observation suggested to the writers that by using hypnosis it might be possible to obtain crucial evidence as to whether the "past-pointing" which is expected by Bárány and his many followers to occur in all normal subjects after bodily rotation (or caloric stimulation of the labyrinth) is a reflex phenomenon or a voluntary act based upon a sensory illusion. On the assumption that the "content of consciousness" can be directly influenced by hypnotic technic, it seemed reasonable to suppose that if past-pointing be due to vertigo it should be possible to prevent this type of reaction by simply suggesting to the subject that he is not dizzy, is not rotating, is perfectly still, etc. On the other hand, if past-pointing be a purely reflex (tonic) reaction, its occurrence should, presumably, be uninfluenced by suggestions of this kind.

In order to verify this latter supposition before undertaking an experiment presupposing its validity, a series of observations were made regarding the effect of hypnotic suggestion upon the knee-jerk and the pupillary reflex. Several male college students, whom we had previously shown to be readily susceptible to hypnosis, were used as subjects. In the case of the knee-jerk, when it was suggested to the subjects that they had no feeling in one of their legs, could not tell when it was touched or tapped, etc., the reaction to a blow on the patellar tendon was, so far as could be detected by simple observation, entirely normal. (When the subjects were told that one of their legs was stiff, could not be moved, etc., the patellar blows had about the same effectiveness as when normal subjects are told to stiffen the leg voluntarily.) In order to test the effect of suggestion on the pupillary reaction, an unlighted electric lamp was held in front of the subjects' eyes in a dimly illuminated room and the subjects were told that they were in complete darkness and could see nothing. While these and similar suggestions were being repeated, the lamp was flashed alternately on and off; but so far as could be determined, the pupillary reflex, like the knee-jerk, was normally prompt and vigorous. In passing, it should perhaps be mentioned that the subjects here used were so deeply hypnotized that when brought out from under the hypnosis they had complete amnesia for the period of the trance; the negative character of the results can therefore scarcely be attributed to any fault in the hypnotic technic.

In earlier, unpublished observations, one of the writers had noted that nystagmus-like movements of the eyes can be produced in hypnotized subjects by telling them, while at rest, that they are being

rotated or that the visual environment is being rotated about them.* Moreover, it had been observed that if a hypnotized subject is asked to close his eyes and is then told that he is whirling around and is very dizzy, he sways, expresses discomfort by grimaces, and not infrequently shows evidences of visceral disturbance, such as blanching and sweating. Since the positive signs of vertigo can thus be induced by hypnotic suggestion in the absence of active vestibular stimulation, it seemed quite likely that James' correspondent had been correct in his contention that actual vestibular vertigo can be abolished, or at least considerably reduced, by this technic. If this be true and if past-pointing be due to vertigo, then it follows, as pointed out above, that it should be possible to prevent this reaction by means of hypnotic suggestions intended merely to eliminate the usual subjective consequences of vestibular stimulation. But if past-pointing be a reflex phenomenon and if all reflex phenomena are as little influenced by hypnotic suggestion as the above observations indicate, the past-pointing should be unaffected by hypnotic technic.

In the hope that it would thus be possible—by showing whether hypnotic suggestion does or does not influence the past-pointing reaction—to determine the origin of this type of response, eight college students (all men) were subjected to the following experimental routine. While still in the normal waking state each subject was first instructed regarding the procedure which would be followed in the administration of the pointing test, care being taken, however, to include no information as to what results might be expected. The subject was then deeply hypnotized and told to get into the rotation chair. (This chair, which has been described elsewhere,[7] was motor-driven, and was started and stopped by specially designed electromagnetic clutches.) As soon as he was in the chair, the subject was blindfolded and was again given the instructions necessary for the proper execution of the pointing test. In order to make certain that he understood these instructions, he was told to extend the arm and index finger so as to touch the finger of one of the experimenters; and at the command, "Point," he was supposed to raise the arm to

*These responses consist of a succession of small saccadic movements in one direction alternating with a large saccadic, or "recovery," movement in the opposite direction. Although possessing a roughly analogous pattern, the hypnotically induced "nystagmus" differs from true vestibular and optokinetic nystagmus in that the slow phase of the latter types of response involves a *continuous* drift of the eyes rather than a succession of rapid, discrete movements. On the other hand, the eye movements observed in the hypnotized subjects are apparently identical with those obtained by telling a normal subject to move his eyes as he imagines he would move them if he or his environment were rotating.

the vertical position and then bring it back as nearly as possible to its original position, so as again to touch the finger of the experimenter. As soon as it was clear that the subject thoroughly understood what was expected of him, he was given the first period of bodily rotation (15 turns in 30 seconds), immediately after which he was commanded to point as previously instructed, then to point again, and then again, the interval between the successive reactions being about three seconds. While one experimenter was thus administering the pointing test, the other experimenter gave continuous suggestions to the effect that the subject was at rest, was not rotating, was not dizzy, etc. After a few minutes' rest the subject was again rotated and when stopped was commanded to point as before, but this time, as he was executing the three pointing commands, he was told that he was very, very dizzy, was going around and around, etc. (No mention was ever made, however, of the direction in which he was supposed to be rotating.) Then followed another period of rotation, after which, as he executed the pointing commands, the subject was told that he was *not* dizzy, etc., and this alternation of positive and negative suggestions following identical periods of rotation was continued until each subject had been rotated six or eight times. In all cases the experimenter who gave the pointing commands held his hand so that the subject always touched it after having raised and lowered the arm; the subject thus received no clew from this source, as to whether or not he was making errors, i. e., past-pointing.

Contrary to what had been expected by the writers, there was no characteristic difference between the pointing reactions which occurred when negative hypnotic suggestions were given and those which occurred when positive suggestions were given. And more perplexing still was the fact that there was no consistency in the responses obtained under either set of conditions. Not only were there great variations in the magnitude of the pointing error from individual to individual and in the same individual from test to test, but there were also frequent inversions in the direction of the error with reference to the direction of the preceding rotation. In fact, the only conspicuous feature of the pointing under either set of conditions was its apparently complete unpredictability.* These surprising results made it obvious that the hypnotic procedure described above could not be satisfactorily used to determine the cause of post-rotational past-pointing. Whether the startling inconsistency of the

*The results obtained by giving the pointing test to hypnotized subjects who were not rotated at all but who were told that they were going around and around were likewise highly variable and inconclusive.

results was in some way due to the fact that the subjects were hypnotized or simply indicated that the past-pointing reaction is considerably less reliable and less constant than many writers seem to imply was a question which obviously demanded further attention.

EXPERIMENT II.

In view of the capricious nature of the findings reported in the preceding section, a new series of observations was undertaken, the purpose of which was twofold. In the first place, it seemed desirable to administer the pointing test to a group of normal subjects under the usual clinical conditions and to obtain an exact quantitative record of their pointing responses, in order to establish a norm or standard of performance with which responses obtained under other, experimentally varied conditions might be compared. The second aim of these observations was to afford a new approach to the question as to whether past-pointing is a voluntary response (in the sense of being a more or less conscious adjustment based upon a sensory illusion) or a reflex. If post-rotational past-pointing results from the subject's feeling that he is turning in the direction opposite to the preceding actual rotation and if it therefore represents merely an attempt on his part to localize a stationary point (viz., the experimenter's finger) with reference to which he believes he is moving, it follows that he should be able to localize with normal accuracy any point which he believes to be rotating with him. If, on the other hand, the past-pointing error is due to a reflex tendency for the arm to be pulled in a particular direction following vestibular stimulation, the direction and magnitude of the error should be the same, regardless of whether the subject is asked to point to an object which he believes to be stationary or to one which he believes to be rotating with him. The following experiment was intended to test these opposed premises.

Twelve healthy college students (all men), without previous experience with the rotation tests, were selected as subjects. That each of them had a normally active labyrinth was determined in advance by the post-rotational nystagmus test. In the experiment proper each man was seated in the rotation chair and, after preliminary instruction, was commanded to make the pointing response three times under each of the conditions described below.

In the first part of the experiment there was placed directly in front of the seated subject a small table, the top of which was just slightly lower than the subject's arm when horizontally extended. On the top of this table a large piece of paper, with a dot located approximately at its center, was fastened down with thumb tacks.

The subject was then given a pencil in his right hand and told to extend his arm and place the point of the pencil on the dot. This done, the subject was asked to close his eyes and raise his arm into the vertical position and then to return the point of the pencil to the dot as nearly as possible and make a small mark. This performance was repeated three times by each subject, with approximately three seconds between the successive trials. Before the subject was allowed to open his eyes, the paper was removed from the table top; and later the magnitude of the "spontaneous" pointing errors to the right or to the left of the original dot was measured in centimeters.* The direction and magnitude of these errors for all twelve subjects are given in the three columns in Table 1, which are headed "Control."

In the next part of the experiment, each subject, with eyes closed, was rotated clockwise for thirty seconds at the rate of one revolution in two seconds, and was stopped so that the table referred to in the preceding paragraph was again directly in front of him. The experimenter immediately moved the subject's hand into a position such that the point of the pencil which he held rested on the dot in the center of a fresh piece of paper. Then the subject, with eyes still closed, was commanded to point three times exactly as in the preceding control tests. The magnitude and direction of the errors made by each subject on the three successive trials are given in the three columns in Table 1 headed "Table—Clockwise Rotation."

After the subjects had been allowed a brief rest, the part of the experiment just described was repeated except that the rotation was in the counter-clockwise rather than in the clockwise direction. The results obtained are indicated in the three columns in Table 1 headed "Table—Counter-Clockwise Rotation."

Following the tests just described, a wooden platform, 20 by 30 inches, was securely mounted in front of the subject on the rotation chair at the same level and at the same distance from the subject as the top of the stationary table had been in the preceding tests. A piece of paper was then fastened on the platform, and the subject was instructed to extend his arm and place the point of the pencil on the dot in the center of the paper. After the subject had been told to close his eyes, the chair was started revolving at the usual speed, in the clockwise direction. As soon as the chair had attained a

*Many ingenious methods of registering the accuracy of the pointing reaction have previously been described—3, 4, 17, 22, 26, 28, 31, 33. The method used in the present study is one of the simplest, but for the purposes at hand was entirely satisfactory.

uniform velocity (which required about five seconds), the subject was commanded to point three times. The subject was then told to open his eyes long enough to enable him to bring the point of the pencil back to the original dot. After the rotation (fifteen turns) had been completed and the subject brought to rest, he was again told to point three times. The results thus obtained, during as well as after rotation, are recorded in appropriately labeled columns in Table 1.

Finally, after another rest interval, the subjects were rotated in the counter-clockwise direction and were asked to point three times following the onset of the rotation and three times following the end of rotation, in the manner described in the above paragraph. The results are recorded in Table 1.

As might have been predicted, the average pointing error for the twelve subjects was small in the control tests, and the individual errors showed no really reliable tendency to occur either to the right or to the left. But it was a source of considerable surprise to the writers to find that following the first period of rotation, in the clockwise direction, the average pointing error was likewise quite small and that the individual errors were by no means uniformly to the right, as the clinical rules for "normal" past-pointing demand. The results obtained after the second period of rotation, this time in the counter-clockwise direction, come nearer to following the orthodox formula; but even here the average deviation is fairly small, and of the twelve subjects four either show no significant error or else past-point definitely in the wrong direction, i. e., to the right.

Post-rotational past-pointing has repeatedly been described in otologic literature as an "invariable" reaction in all normal subjects; the results just referred to are obviously grossly incompatible with such an interpretation. Moreover, a survey of the writings of the relatively few investigators who have studied the pointing reaction experimentally clearly shows that the results obtained by the present writers are not at all exceptional. As early as 1919, Malan[21] reported that ostensibly normal subjects frequently show an inverse or otherwise highly irregular past-pointing reaction. Three years later Benjamins[5] reported that of 55 normal subjects tested by him, only 16 regularly past-pointed in the direction of the preceding bodily rotation. Of the remaining subjects 12 showed a consistent inversion of response, and the other 27 were "mixed types." In 1925 Roorda[25] reported that of 52 normal subjects which he systematically tested for past-pointing, 16 failed in one way or another to conform with the traditional clinical expectations. A year after the publication of

TABLE 1

Subject	Control			Table—Clockwise Rotation			Table—Counter-Clockwise Rotation			Board—Clockwise Rotation			Board—Clockwise Rotation Post-Rotation			Board—Counter-Clockwise Rotation			Board—Counter-Clockwise Rotation Post-Rotation		
	1st trial	2nd trial	3rd trial	1st trial	2nd trial	3rd trial	1st trial	2nd trial	3rd trial	1st trial	2nd trial	3rd trial	1st trial	2nd trial	3rd trial	1st trial	2nd trial	3rd trial	1st trial	2nd trial	3rd trial
Heb.	R 0.9	R 2.0	R 2.8	R 5.6	R 6.1	R 5.6	L 1.7	L 5.7	L 6.2	R 5.4	R 5.4	R 7.7	L 1.9	L 5.6	L 8.6	L 8.2	L16.0	L19.0	L 2.0	R 3.7	R 3.0
Rab.	L 3.4	L 3.6	L 2.7	L 0.7	L 7.1	L 7.7	L12.1	L22.1	L25.3	R 9.3	R11.8	R17.1	L 5.4	L10.8	L10.3	L 5.2	L 8.0	L13.2	L 2.3	L 4.1	L 4.9
Buc.	R 1.0	L 1.3	L 1.3	L 2.2	L 1.2	L 4.1	L 8.5	L 5.1	L10.4	R16.0	R12.3	R10.4	L13.3	L12.9	L13.4	L 4.4	L 2.1	L 1.9	R 5.8	R 7.4	R 9.9
Rom.	R 2.7	R 3.7	R 4.1	R 1.1	R 2.3	R 2.7	L 7.9	L 7.2	L 5.8	L 3.1	L 1.6	L 6.3	L 2.9	L 1.1	L 5.2	L 3.4	L 7.7	L 9.2	L15.6	L16.2	L14.0
Sol.	L 2.7	L 4.0	L 4.7	L 5.6	L 8.3	L 9.5	L13.2	L 9.1	L 9.9	L 4.8	L 5.1	L 6.6	L 6.8	L10.8	L15.5	L11.8	L13.9	L14.9	L14.1	L16.2	L11.5
Ull.	L 0.6	L 2.8	L 5.4	L10.2	L11.6	L13.5	R 2.6	R 5.2	R 5.9	L10.6	L 4.0	L 1.7	L13.2	L16.5	L20.0	L12.0	L17.6	L28.8	L 6.1	L 9.0	L 9.7
McD.	R 1.1	R 2.3	R 2.6	R16.5	R18.3	R24.8	L10.6	L 3.7	0.0	R 8.3	R19.7	R26.5	R 1.9	L11.3	0.0	R13.5	R15.5	R24.7	L 2.2	L 3.7	L 5.0
Dab.	L 0.6	L 5.6	L 7.4	R 8.7	R 8.5	R 3.7	L 0.6	R 0.3	R 1.7	R13.5	R14.2	R21.7	R 1.9	R 2.1	0.0	R 5.1	R 7.0	R11.9	R 7.0	R 6.1	R11.1
Sha.	L 2.3	L 2.3	L 2.7	R 1.7	L 2.7	L 3.1	L 2.2	L 0.8	L 2.3	0.0	R 1.8	R 3.9	L10.2	L19.0	L19.7	L18.1	L26.6	L30.6	L 2.1	L 7.2	L12.0
Lot.	L 1.3	L 1.6	L 1.1	R 2.6	R 0.1	L 0.9	R 2.1	R 4.8	R 7.1	R 3.8	R 6.3	R 8.6	L 0.5	L 0.9	L 3.0	R 0.8	R 1.7	R 5.0	L 4.3	L 1.4	R 1.0
Pra.	R 0.3	R 1.8	R 4.9	L 5.1	L 5.7	L 6.8	R 1.1	R11.7	R16.3	R 6.6	R10.0	R12.1	L 1.7	L 2.7	L 3.6	R 3.6	R 7.1	R 7.7	R 2.0	R 1.9	R12.0
Dau.	L 3.1	L 5.0	L 5.7	L 3.2	L 7.9	L 7.9	L 2.5	L 1.8	L 5.0	R 0.7	L 3.5	L12.8	L 1.8	L 5.2	L 6.1	R 3.5	R 5.5	R 3.1	L 0.3	L 1.7	L 5.1
Gross Total	20.3	36.0	45.1	63.5	83.1	90.9	70.9	80.5	95.9	82.1	99.0	135.1	68.6	102.2	120.2	89.9	128.7	170.0	64.1	78.9	102.5
R—Total	6.0	9.8	14.4	36.2	35.6	36.8	8.8	25.0	31.0	63.6	81.5	108.0	4.9	2.1	0.0	26.8	36.8	52.4	14.8	19.4	37.0
L—Total	14.3	26.2	31.0	27.3	47.5	54.1	62.1	55.5	64.9	18.8	17.5	27.1	63.7	100.1	120.2	63.1	91.9	117.6	49.3	59.5	65.5
Net Total	L 8.3	L16.4	L16.6	R 8.9	L11.9	L17.3	L53.3	L30.5	L33.9	R14.8	R61.0	R80.6	L58.8	L98.0	L120.2	L36.3	L55.1	L65.2	L34.5	L40.1	L28.5
Net Average	L 0.69	L 1.37	L 1.39	R 0.74	L 0.99	L 1.44	L 1.41	L 2.54	L 2.83	R 3.73	R 5.33	R 6.72	L 1.90	L 8.17	L10.02	L 3.03	L 4.59	L 5.43	L 2.88	L 3.34	L 2.38

Pointing errors made by 12 normal subjects under the various experimental conditions indicated in the column headings. All entries represent **absolute** pointing errors, i. e., distance (in centimeters) from the original starting, or "null," point. **L** or **R** before an entry indicates whether the error is to the left or to the right of this point. The **relative** pointing error, i. e., the deviation from one trial to the next, can be obtained for the 2nd and 3rd trials, respectively, by subtracting the 1st absolute error from the 2nd and the 2nd absolute error from the 3rd (adding where the signs are different). On the 1st trial, the absolute error and the relative error are, of course, identical.

TABLE 2

Subject	Control		Response Made Following Acceleration				Response Made Following Retardation				Control	
			Counter-Clockwise Rotation	Clockwise Rotation	Counter-Clockwise Rotation	Clockwise Rotation	Clockwise Rotation	Counter-Clockwise Rotation	Clockwise Rotation	Counter-Clockwise Rotation		
	Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7	Test 8	Test 9	Test 10	Test 11	Test 12
Deg.	R 3.2	L 1.0	R 6.1	L18.2	R 7.9	L 9.3	R 1.6	L12.2	R10.8	L10.9	L 1.0	L 0.2
Smi.	R 1.1	R 1.0	R22.2	L 7.2	R22.2	L23.6	R 1.1	L 4.0	R 8.1	L 2.1	R 1.2	R 2.0
Moy.	R 1.8	R 1.1	R15.0	L16.1	R14.5	111.1	R 5.7	L 1.9	R 7.1	L 1.1	R 0.9	R 2.1
Wer.	R 0.9	R 0.1	R21.0	L23.1	R24.1	L23.8	R 4.5	L 1.1	R 1.1	L 2.1	R 1.3	R 1.6
Lea.	L 1.6	R 0.2	R13.0	L10.0	R 6.2	L 8.2	R 1.0	L 6.8	R 1.1	L 5.7	L 3.3	L 1.1
Wat.	R 1.0	R 3.8	R13.1	L20.5	R16.1	L15.5	R 2.7	L 7.2	R 1.7	L 8.1	R 0.7	R 1.7
Gra.	L 5.0	R 0.1	R20.2	L26.1	R26.0	L21.3	R 7.1	L 4.4	R 1.9	L 7.1	R 0.2	R 0.7
Hes.	R 1.5	L 0.6	R13.5	L20.0	R11.0	L16.5	R 1.6	R 1.1	L 5.8	L 0.8	R 2.3	R 1.6
Wal.	L 3.5	L 1.0	R14.2	L25.0	R12.2	L18.7	R 4.8	R 0.4	R 2.1	L 0.2	R 0.6	R 2.4
Lev.	L 0.7	R 1.1	R14.8	L17.8	R12.1	L19.7	L 3.0	L 4.8	L 1.3	L 5.2	L 0.2	L 0.8
Woo.	L 4.2	L 1.2	R18.8	L15.6	R11.3	L12.3	L 0.3	L 6.5	R 0.2	L 3.3	L 5.8	L 3.8
Gro.	L 4.5	L 3.4	R16.3	L25.0	R 7.3	L23.2	R 7.2	L15.0	R25.0	L 4.3	R 1.9	L 0.4
Gross Total	32.3	15.2	189.5	225.2	171.2	206.5	43.9	72.0	72.8	54.5	19.4	21.7
R—Total	12.8	8.0	189.5	0.0	171.2	0.0	10.6	1.8	71.5	0.0	9.1	12.1
L—Total	19.5	7.2	0.0	225.2	0.0	206.5	3.3	70.2	1.3	54.5	10.3	9.6
Net Total	L 6.7	R 0.8	R189.5	R225.2	R171.2	L206.5	R37.3	L68.4	R70.2	L54.5	L 1.2	R 2.5
Net Average	L 0.56	R 0.07	R15.79	L18.77	R11.27	L17.21	R 3.11	L 5.70	R 5.85	L 4.54	L 0.10	R 0.21

Measures of the tonic imbalance in the musculature of the arms in 12 normal subjects, as recorded under the conditions indicated in the column headings by the apparatus shown in Fig. 1. Each entry indicates (in centimeters) the amount by which the recording planchette had deviated laterally by the time it had completed its upward excursion. **L** or **R** before an entry indicates whether this deviation was to the left or to the right of the true center of the sheet of paper on which the excursion of the planchette was recorded.

Roorda's study, Xanthakos[xiii] described an investigation in which 100 healthy persons were tested for past-pointing. Of this group 54 showed so-called "normal" reactions; the remaining 46 persons showed anomalies of one kind or another. Then in 1927, Lipschütz[19] reported that he had been able to obtain "normal" pointing reactions in only 6 out of 32 healthy subjects. And these experimental results have been confirmed, moreover, by the clinical experience of Kopetzky and Almour,[18] Froment and Mayoud,[13] and others!

In the light of the findings of the authors just cited and of the results obtained by the present writers, it is difficult to avoid the suspicion that clinical practitioners who have used the post-rotational pointing test must have frequently done so (unless deceived by traditional dogmas and lack of personal experience) more with a view toward impressing their patients than with the hope of securing information of genuine diagnostic value. As shown above, the magnitude of the post-rotational pointing error is often so small and the direction so imperfectly correlated with the direction of the preceding rotation in perfectly normal subjects that it is not easy to see how the test can have any clinical significance whatever.* Since these peculiarities are so commonly manifested by healthy subjects, their presence in persons suspected of having pathologic labyrinths or neural lesions would seem to be quite devoid of dependable diagnostic implication. The writers are far from denying that the accuracy of the pointing reaction is disturbed by vestibular stimulation; their insistence is merely that the results of the post-rotational pointing test—as ordinarily administered—fall far short of possessing the degree of predictability commonly claimed for them; and since clinical diagnosis is an *individual*, not a *statistical procedure*, this shortcoming would seem to render the test practically worthless for clinical purposes.

So far as the writers are aware, no attempt has previously been made to test the pointing reaction *during* bodily rotation, i. e., under conditions such that the subject knows that the object toward which the pointing reaction is directed is, of necessity, rotating concurrently with his own body. On the basis of the traditional rules for post-rotational past-pointing it would be expected that *rotational* past-pointing would occur in the direction opposite to that of the bodily move-

*Certain writers,[12 19] who recognize the unreliability of the post-rotational pointing test continue to use the pointing test with caloric stimulation of the labyrinth; whether the past-pointing reactions obtained under the latter conditions are any more significant than those elicited after rotation, the present writers are not prepared to say.

ment, providing that the pointing error is caused by a reflex vestibular effect on the muscles of the arm; if, however, the pointing error is due to vertigo, there should be virtually no past-pointing during rotation under the conditions just described. It was therefore something of a surprise that of the twelve subjects tested for pointing by the present investigators during the clockwise rotation, eight of them, instead either of past-pointing in the direction opposite to that of the bodily rotation (i. e., to the left) or of not past-pointing at all, showed a definite pointing error in the *same* direction as that of the bodily rotation (i. e., to the right). That this "inversion" of the pointing error might represent a real reaction tendency, instead of being due merely to the unreliability of the response, is suggested by the fact that during counter-clockwise rotation comparable results were obtained: here seven of the twelve subjects showed an inverse pointing reaction. *Following* the period of clockwise rotation —where the subjects likewise knew that if they were turning, the object they were trying to touch must also be turning—11 of the 12 subjects showed inverse past-pointing. However, following the period of counter-clockwise rotation, eight of the twelve subjects past-pointed, under essentially the same conditions, in the "normal" direction, thus interrupting the somewhat consistent tendency toward inverse past-pointing noted in the other observations.

The results of this latter test, taken in conjunction with the results of the preceding three tests, make it seem highly probable, therefore, that the past-pointing reaction is quite as unreliable and variable, both as regards magnitude and direction, when the subject knows that the object toward which the reaction is directed has to move if he moves as is the past-pointing reaction when the subject knows that the object must remain stationary, no matter how he himself moves. For reasons already stated, this conclusion is quite inconsistent with the view that past-pointing is due to vertigo. It might also be said that this conclusion opposes likewise the view that past-pointing is due to a vestibular reflex (tonic) effect upon the arm muscles. In fact, it might even be argued that this conclusion tends to imply that vestibular stimulation has no effect whatever upon the pointing reaction. These two latter inferences, however, do not logically follow nor are they supported by the experimental facts, as is indicated below.

An analysis of the data presented in Table 1 reveals that the so-called spontaneous pointing error is usually decidedly smaller than the pointing error which appears when the individual has been subjected to vestibular (rotational) stimulation. This difference is clear-

ly and consistently evident between the "Gross Totals" for the "control" tests and those for the "rotation" tests. This comparison shows convincingly that vestibular stimulation does significantly affect the *magnitude* of the pointing error (i. e., increases it), even though the *direction* of the error obeys no consistent formula. Lipschütz[19] has similarly noted that the errors occurring after bodily rotation "are very much greater than those occurring in the spontaneous tests"; but he, too, called attention to the fact that in neither case can the direction of the error be confidently predicted.* In the following section an explanation for these apparently paradoxical results will be offered and an experiment described which was designed to test its validity.

EXPERIMENT III.

Regardless of which of the various conditions described above is employed in giving the pointing test, the reaction is always executed with an *external,* or *objective,* spatial reference. Assuming, now, that vestibular stimulation does tend to pull the arm in one direction or another, this pull will normally be perceived by the subject through proprioceptive cues; and since the pointing reaction has an external reference, the subject—in order to come as close as possible to touching the object toward which the pointing reaction is directed—will naturally try to correct, or compensate, for the vestibular reflex effect upon the arm. When this compensation is inadequate, the subject past-points in the "normal" direction. But when the compensation is over-emphasized (as apparently frequently happens), the subject shows an "inverse" pointing error. If these premises are correct, it follows, therefore, that the vestibular reflex effect upon the arm should be more conspicuously manifest and more perfectly correlated with the type of vestibular stimulation employed to produce it if the subject be asked to execute some arm movement which has *no external reference* instead of the conventional pointing reaction.

In order to test this deduction, the writers constructed an apparatus which was originally designed by Dr. J. Q. Holsopple,

*Since the *magnitude* of the pointing error thus appears to be definitely affected by vestibular stimulation, it might be argued that it would afford a more reliable clinical index to vestibular activity than the *direction* of the pointing error, which has been shown above to be virtually worthless in this connection. Unfortunately, however, magnitude of error is merely statistically, not invariably, greater with than without vestibular stimulation; and clinical diagnosis, as pointed out above, is an individual matter.

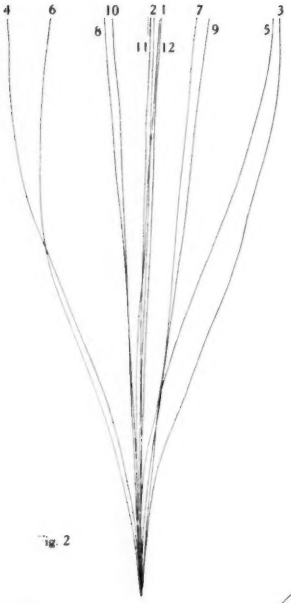

Fig. 2

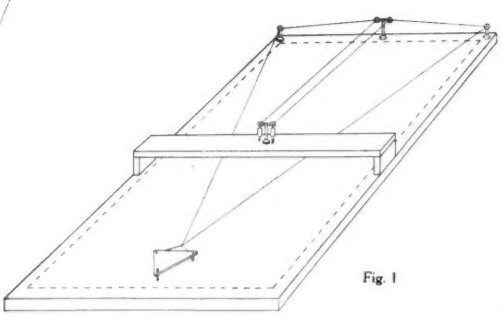

Fig. 1

Fig. 1. Diagram of apparatus for testing tonic imbalance in the musculature of the arms. The subject grasps the wooden pendants, y and x, between the thumb and fingers of the right and left hands, respectively; and, upon command, moves the extended arms outward in the horizontal plane. This causes the metal planchette, which is connected to the pendants by strings as indicated in the diagram, to move upward on the inclined baseboard, leaving on the large sheet of paper (indicated in the diagram by the broken lines) a pencil line record of its entire excursion. If the two arms move outward at the same speed, the planchette glides straight up the incline; but if one arm moves more rapidly than the other, the planchette deviates laterally, toward the side of the more rapidly moving arm. After each upward excursion, the planchette is returned by the experimenter to a v-shaped holder (not shown in the diagram) which is centrally located near the bottom of the baseboard and which insures that the planchette always starts its excursion from the same point. In Fig. 2 may be seen the type of records obtained with this apparatus under the various experimental conditions described in the accompanying legend.

Fig. 2. Examples of records obtained with the apparatus shown in Fig. 1. The individual lines are numbered to correspond with the 12 tests given under the various conditions described in the column headings in Table 2. Thus, lines 1, 2, 11 and 12 represent "control" reactions. Lines 3 and 5 and lines 4 and 6 represent reactions which occurred during counter-clockwise bodily rotation and during clockwise rotation, respectively. Lines 7 and 9 and lines 8 and 10 represent reactions which occurred immediately after clockwise rotation and immediately after counter-clockwise rotation, respectively. The particular set of records here reproduced is for the subject designated in Table 2 as "Moy." This set of records was selected for purposes of illustration because it portrays so perfectly—both as regards direction and magnitude of the deviation of the individual lines from the true center of the record sheet (indicated by the short dotted line)—the general reaction tendencies of the entire group of subjects, as revealed by the "Net Averages" in Table 2. Virtually all of the other eleven sets of records show, however, the same general pattern.

Chief Clinical Psychologist for the New Jersey State Department of Institutions and Agencies, but which has not previously been described in print. This apparatus, which is diagrammatically illustrated in Fig. 1, consists essentially of an inclined plane, 24 inches wide and 36 inches long, which can be fastened firmly to the rotation chair, mentioned above, directly in front of the subject and so located as to slope upward and outward at an angle of approximately 45°. The subject grasps the two wooden pendants, *y* and *x*, between the thumb and fingers of the right and left hands respectively, and, upon command, moves the extended arms outward in the horizontal plane. This causes the metal planchette to move upward, leaving a pencil-line record on the piece of paper indicated in the illustration by the broken lines. If both arms move outward with equal speed, the planchette moves directly upward on the sheet of paper. If, however, as a result of tonic imbalance or for any other reason, one of the arms moves outward more rapidly than the other, the planchette deviates laterally in its ascent, to the right or to the left, depending upon which arm moves the faster. As the planchette nears the top of the incline, the strings connecting it to the two pendants become taut and the movement of the subject's arms is automatically stopped.

In the series of observations made by the present writers with the apparatus just described, twelve college students (three women and nine men), none of whom had had previous experience with rotation tests, were used as subjects. Each subject was seated in the rotation chair and, after having been shown to possess a normal post-rotational nystagmus, was blindfolded. His arms were then brought forward into an extended horizontal position so that he grasped the two pendants, one with each hand. The subject was next commanded to move the two arms outward simultaneously and as nearly at the same speed as possible, the whole response to require only about one second. The entries presented in Table 2 in the column headed "Test 1—Control," represent the amount (in centimeters) by which each of the twelve subjects caused the planchette to deviate to the right or to the left by the time it had completed its excursion, i. e., reached the top of the inclined plane. Although slight individual deviations are here evident, there is no consistent tendency to deviate either to the right or to the left, as is indicated by the smallness of the "Net Average."

After the planchette had been returned to the starting position the test was repeated under exactly the same conditions. The amount of deviation shown by each of the twelve subjects is recorded in the column in Table 2 which is headed "Test 2—Control." Again the

"Net Average" reveals no greater tendency for the deviation to occur in one direction than in the other.

(Later, following the eight tests described immediately below, two more "control" tests were made. These are referred to in Table 2 as "Test 11" and "Test 12." The results, it will be noted, are quite similar to those obtained on "Test 1" and "Test 2.")

Following the first two tests, each subject was rotated in the counter-clockwise direction at the standard speed of one revolution in two seconds. Before the onset of rotation the subject was instructed to be prepared to move the arms outward upon command, and this command was given as soon as acceleration had been completed and a uniform rate of rotation attained. Under these conditions the deviation of the planchette was to the *right* in all twelve subjects and was of very considerable magnitude, as is revealed by the figures given in the column headed "Test 3—Counter-Clockwise Rotation" in Table 2. After a few minutes' rest the test just described was repeated, except that the rotation was now in the clockwise direction. Again the deviation of the planchette was consistently in one direction, but this time to the *left*. The magnitude of deviation was about the same as in the preceding test. The individual results for this test are given in the column headed "Test 4—Clockwise Rotation."

Tests 5 and 6 are duplicates of tests 3 and 4, respectively. Reference to the appropriate columns in Table 2 will show that the results obtained are strictly parallel to those described in the foregoing paragraph.

In tests 7, 8, 9 and 10 each subject was rotated at the standard speed for 30 seconds and then, immediately after being stopped, was told to execute the outward movement of the arms. In tests 7 and 9, where the rotation was clockwise, the deviation of the planchette was to the right in 21 out of 24 cases. In tests 8 and 10, where the rotation was counter-clockwise, the deviation of the planchette was to the left in 22 out of 24 cases. Thus, in these four tests, as well as in the four preceding tests where the reaction was made just after acceleration instead of just after retardation, there is an almost perfect correlation between the direction of the rotation stimulus and the direction of the deviation of the planchette (see Fig. 2 and the accompanying legend).

The consistency of the above results—obtained under conditions wherein the arms are moved without reference to any point outside the subject's own body—seems clearly to indicate that stimulation of the vestibular receptors by bodily rotation normally produces definite

tonic imbalance in the muscles of the arms.* There can apparently be no doubt that in the clinical situation in which the pointing reaction is tested after a period of bodily rotation this reflex disturbance of tonus is present. Here, however, the subject is called upon to execute an arm movement which has a definite external reference and, feeling the proprioceptive stimulation produced by the tonic disturbance in the arm muscles, more or less consciously trys to compensate for this state of imbalance. This means that in the traditional post-rotational pointing test the real vestibular manifestations are largely overlaid and distorted by uncontrolled influences, with the result that, although the magnitude of the pointing error is usually somewhat

*Dusser de Barenne,[8] Magnus,[20] Beritoff[6] and other writers have advanced convincing evidence that in many quadrupeds rotational stimulation of the vestibular receptors produces specific reflex movements of both the fore- and hind-limbs. These responses are always in the direction opposite to the angular acceleration affecting the labyrinth and can be plausibly interpreted as directly assisting in the maintenance of postural equilibrium, especially during passive bodily tilting or active locomotion. In the case of organisms which have assumed an upright posture and bipedal locomotion, the only equilibratory function which the fore-limbs, or arms, fulfill is that they are frequently used as balancing devices and also serve to catch the individual in falling. These two types of reaction are antagonistic and are probably mediated by quite different neurosensory mechanisms. If, for example, a person feels himself tilting slightly forward but in no imminent danger of falling, he is likely to swing the arms *backward* in order to re-establish his balance. Here the arms move (in the rotational sense) in the *same* direction as that of the angular acceleration which is affecting (probably only very slightly if at all) the vestibular receptors; the movement, therefore, is almost certainly not prompted by vestibular stimulation. But if it is evident that a fall in the forward direction is inevitable (under which conditions the movement of the head is more rapid and the vestibular stimulation more intensive), the person will throw his hands out *forward;* this latter response is in the direction *opposite* to that of the acceleration which is affecting the vestibular apparatus and may, therefore, be a member of the same class of responses as the vestibular limb-reflexes which have been demonstrated in quadrupeds. Granting, then, that vestibular arm-reflexes may be of distinct advantage whenever a person falls forward, backward or sidewise, it is difficult to see how in adult human beings the arm-reflex to bodily rotation around the long axis of the body (i. e., in the horizontal plane) can have any biologic utility whatever. It is conceivable that this reflex may be a phylogenetic survival from the days when man's progenitors regularly progressed on all fours. This, of course, is inconsistent with the growing modern view that all responses, reflex and otherwise, are developed to meet specific individual, or ontogenetic, demands (but many other well established observations are also quite inconsistent with this hypothesis!). On the other hand, the fact that during prenatal and early postnatal life the human organism tends to recapitulate the locomotive evolution of the race—from swimming-like movements to crawling, and from crawling to upright walking—may account for the original development and persistence into adulthood of vestibular arm-reflexes which have functional significance only at early stages of ontogeny. In any event, it seems fairly certain that such reflexes do exist. What their origin and explanation is cannot at present be determined, except by inference and speculation.

greater following vestibular stimulation than under ordinary conditions, the direction of the error is very imperfectly correlated with the direction of the preceding bodily rotation.

Why the lateral deviation of the planchette in the tests just described should have been so much greater when the arm movements were executed just after acceleration than when executed just after retardation (see Fig. 2) is not clear to the writers. The time required for acceleration was in all cases roughly equal to the time required for retardation (i. e., approximately five seconds), so that difference in the intensity or duration of the resulting vestibular stimulus-effects cannot account for the difference regularly observed in the overt reactions. (The interval between the acceleration and the retardation was sufficiently long—approximately twenty-five seconds—presumably to prevent the effects of the former from counteracting the effects of the latter, which, of course, normally occurs when the rotation is of much briefer duration.) It is true that in the particular experimental procedure here used the four tests which were given following acceleration preceded the four tests which were given following retardation; and it is also true that certain writers,[14,15] have noted that with repeated bodily rotation the post-rotational pointing reaction tends to become habituated, i. e., progressively decreases in magnitude. That habituation cannot, however, be responsible to any significant degree for the difference in the results obtained in the planchette test under the two sets of conditions mentioned is indicated, first of all, by the fact that the decrease in magnitude of deviation occurs *abruptly* with the transition from the one test situation to the other, not progressively. Moreover, after the subjects had been given the planchette test under the various conditions indicated by the column headings in Table 2, they were occasionally again rotated and given the planchette test immediately after acceleration; the magnitude of the resulting deviation was nearly always considerably greater than the magnitude of the deviation observed following retardation.

Mechanical factors—notably, centrifugal force and air resistance—have also been considered as possible explanations of this difference in magnitude of deviation. Anyone who has tried to move his arms or legs during bodily rotation at the rate here used knows that centrifugal force exercises a clearly perceptible influence upon the attempted movement; in many types of movement the customary coördinations are definitely disturbed and have to be consciously and carefully modified in order that the movement achieve the desired end. However, it is not easy to see how centrifugal force, which acts *radially*, could affect the arms during their outward movement in the

planchette test in such a way as to cause them to deviate *tangentially*, in the direction opposite to that in which the subject is rotating. Air resistance undeniably exerts a force upon the extended arms during bodily rotation, tending to make them "lag behind"; but its influence must be so slight at the speed of one revolution in two seconds as to render it quite negligible. The obvious solution to the problem as to whether the greater lateral deviation of the arms during rotation is merely a mechanical artifact, perhaps of unsuspected origin, or is a true physiologic phenomenon would be to give the planchette test, both following acceleration and following retardation, to individuals whose labyrinths are known to be "dead." Following retardation such persons would presumably show no greater deviation of the arms than under ordinary circumstances; if, however, following acceleration these subjects showed a reliable tendency for the arms to deviate in the direction opposite to that of the bodily rotation, it would be evident that the deviation had a nonvestibular, mechanical origin, which would account for the difference noted above in the magnitude of the deviation shown by normal subjects following acceleration and following retardation. Unfortunately, individuals with inactive labyrinths have not been available to the present writers. Until tests of the kind just mentioned have been carried out, the real cause of the difference in results just referred to must apparently remain undetermined.

(Since the manuscript of this article went to press, Professor Raymond Dodge has suggested to us what appears to be the explanation of the anomaly discussed in the two preceding paragraphs. When the planchette is in its starting position, at the base of the inclined plane, it is fairly near the axis of rotation and its linear velocity (spatial displacement per unit time) is relatively small. As the planchette ascends the incline, its distance from the axis of rotation increases; and since the angular velocity of the subject, the chair, and the attached apparatus is constant, the planchette is subjected to a linear acceleration as the radius of its rotation increases. During this period of linear acceleration, the planchette, by virtue of its inertia and non-rigid suspension, tends to "lag behind," thus deviating in its upward course on the incline in the direction opposite to that of the rotation. Following rotation, when the subject, chair, and attached apparatus have no angular velocity, there is no increase in the linear velocity of the planchette as it glides up the incline. Any lateral deviation observed under these latter conditions can, therefore, be attributed only to physiologic factors; the lateral deviation of the planchette during rotation is, on the other hand, due to physiologic factors plus the mechanical factor just described. This explanation seems to account most adequately for the discrepancy noted under these two sets of conditions in the magnitude of the lateral deviation of the planchette in its ascent of the inclined plane.)

DISCUSSION.

If the results obtained in Experiment III by means of the apparatus shown in Fig. 1 prove to be typical, it will obviously be possible

by this new technic to obtain a more reliable index of vestibular normality than the traditional pointing test provides.* However, the nystagmus test, when used with certain cautions (which have been emphasized elsewhere[23]), provides such a simple and convenient check on the integrity of the vestibular receptors that a vestibular arm-reflex test—even though perfectly reliable—would be largely superfluous unless it afforded something more in the way of diagnostic clues than does the nystagmus test. Following a lead suggested by Bárány, Jones[17] has developed the thesis that the pointing test achieves its major usefulness, not in determining the functional status of the vestibular receptors as such, but rather in showing whether the pathways which normally mediate the neural impulses responsible for the occurrence of post-rotational past-pointing are intact. Jones took the position that, whereas nystagmus is "a simple reflex," the pointing reaction is "a cerebral act of orientation" and that vestibular past-pointing occurs, not because of tonic or reflex acts, but "because of *vertigo*."†

*Bárány[2] has described a modified pointing test, called the "Einstellungsversuch," which bears a certain superficial resemblance to the new test described above but which is fundamentally quite different. In the revised Bárány test the subject is told to close his eyes and extend the arm forward and rest the end of his forefinger on the forefinger of the experimenter. The subject is next commanded to move the arm far outward in the horizontal plane and then to return it inward to the point where the subject imagines the experimenter's finger to be. In the meantime the experimenter has withdrawn his finger, and the extent by which the subject fails to return his finger to its original position is regarded as the test error. Although the writers have had no experience with this test, it would appear to have the same disadvantages as the conventional form of the pointing test—i. e., the arm movements are executed with a definitely external reference and, following bodily rotation, are probably affected by the same conscious influences as are above shown to affect the conventional postrotational pointing reaction.

†Italics here and in the following quotation are the author's.

"It may be regarded as a law of the ear-tests," says this writer, "that where *there is no vertigo there is no past-pointing*. Vertigo is the primary reaction: past-pointing is a secondary manifestation. Anyone wishing to understand this phenomenon need merely have himself turned in the chair. After he is turned to the right he has, on stopping, a subjective sensation of turning to the left. He feels that he is leaving the examiner behind, and *for this reason* he consciously and deliberately points to the right, where he conceives the finger now to be. . . . An intelligent person who knows that he would naturally past-point after stimulation, can voluntarily by a careful calculation correct the past-pointing and deliberately point in the other direction. . . . This proves conclusively the mental control over the direction of the pointing. . . . S. A. Brumm has demonstrated that after turning, if the individual is asked to move his finger up and down in a vertical plane, he is able to do so and does not deviate to the side. He merely moves his finger up and down in front of him in the vertical plane which he conceives to be revolving with him. If, however, he touches some *external object*, and then tries to find it again, he feels that he is leaving that object behind him and past-points in that direction." pp. 187-188.

Jones described the "tracts producing vertigo . . . as extending from the ear, through the eighth nerve, through the brain stem, and through the cerebellar peduncles as far as the cerebellar nuclei." He assumed that further tracts relay the vertiginous impulses from the cerebellum to the cerebrum, where these impulses are so integrated as to lead to past-pointing or not, depending upon the way in which the subject consciously evaluates them. The most obvious inference from the foregoing would seem to be that the presence or absence of post-rotational past-pointing indicates simply whether the subject regards the post-rotational sensations of bodily movement as real or illusory. But Jones assumed that all näive (i. e., subjects without special and intimate knowledge of the effects of bodily rotation) would regard these sensations as real and that the absence of post-rotational past-pointing in such subjects unequivocally indicates (providing the nystagmus test shows the vestibular receptors to be sound) impairment of the neural tracts which he thought of as normally bringing the vertigo-producing impulses into consciousness.

The results obtained in Experiment II of the present study and the findings of various other writers cited above show, first of all, that a large percentage of normal näive subjects *do not* past-point following bodily rotation in the manner characterized by Jones as practically invariable. Moreover, the results of Experiment II also indicate that post-rotational vertigo, instead of being interpreted as real bodily rotation, is apparently usually regarded by the subject as an illusion. This means that his conception of the actual spatial relations existing between himself and the object toward which the pointing reaction is directed is more or less accurate, as evidenced by the fact that "inverse" pointing errors are just about as common as errors in the direction designated by clinical tradition as "normal."* As is revealed by the results of Experiment III, the main

*Fischer and Wodak,[9 10 11 29 30 31] have expressed the belief that the post-rotational pointing reaction is influenced both by vertigo and by reflex vestibular effects upon the muscles of the arm. The present writers do not deny that it is possible to create experimental conditions in which it is difficult for the subject to differentiate between vertigo and sensations of actual bodily rotation. Under such conditions vertigo, being perceived as true bodily movement, would undeniably affect the post-rotational pointing response as conventionally tested. However, the fact remains that in most experimental and clinical situations there are sufficient nonvestibular cues present during actual rotation—air currents, the changing direction of auditory stimuli, noise and vibration from the rotation of the chair, etc.—to enable the average subject, however unfamiliar with the effects of bodily rotation, to know fairly accurately when his sensations of bodily rotation are real and when illusory. As previously mentioned, the rotation chair used in the present

if not the exclusive effect which vestibular stimulation has upon the pointing reaction is apparently achieved by a much more direct mechanism than the one postulated by Jones and is wholly independent of vertigo.† Although the exact nature of this mechanism cannot be definitely stated at present, there are two likely possibilities. It is conceivable, on the one hand, that the vestibular impulses responsible for this effect pass directly from the vestibular receptors to the arm muscles (probably over the vestibulospinal tract[24]) and therefore influence the voluntarily produced arm movements involved in pointing in a more or less mechanical manner, i. e., by setting up reflex tendencies in the muscles, which are prone to distort the voluntarily initiated response. On the other hand, it is also conceivable that the impulses produced by vestibular stimulation are integrated at a fairly high (but unconscious) level with the voluntarily initiated impulses and in this way alter the final overt response. But regardless of which of these neural mechanisms is the one actually involved here, it seems fairly certain that whenever, as a consequence of vestibular stimulation, a voluntary arm movement is interfered with, or distorted in any way, this interference is sensed proprioceptively by normal subjects. Whether an attempt will then be made to correct or compensate for this interference appears to depend in a large measure upon the particular circumstances under which the arm movement is being executed.

When the voluntary movement of the arm is executed with an external reference, as is the case in the traditional pointing test, the subject feels constrained to compensate for the vestibularly produced

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investigation was started and stopped by the use of electromagnetic clutches. This meant that the motor which was used to drive the chair could be started before the onset of the rotation of the subject and could be allowed to continue running for an indefinite time after the subject was brought to rest. Advantage was regularly taken of this possibility of eliminating one cue to whether the sensations of bodily rotation were real or illusory; but so many other cues remained that the subjects apparently had no difficulty in usually differentiating between the two conditions quite accurately.

†By "wholly independent of vertigo" we mean that the pointing reaction is probably not ordinarily influenced by sensations (if any) resulting directly from vestibular stimulation. The fact is, the evidence seems to indicate that the causal relationship here is in the reverse direction: the perception of passive bodily rotation (vision excluded) as well as the postrotational illusion of bodily movement (vertigo) are much affected by, if not entirely dependent on, the muscular reactions and tonic changes reflexly initiated by the vestibular stimulation. This supposition is strongly supported by the experimental findings of Travis and Dodge (26a) and by evidence cited by Mowrer (22a).

lateral deviation of the arm (which he senses proprioceptively), thus more or less masking the real vestibular manifestation. Contrary to Jones' contention that all näive subjects regard the sensation of post-rotational vertigo as *real*, the present writers believe that at least the majority of so-called näive subjects know these sensations to be *illusory* and try, by means of the type of compensation just referred to, to overcome the disturbing effect of the vestibular stimulation upon the arm musculature and to point accurately to the designated external object. If this compensation is inadequate, there is past-pointing in the direction expected by clinicians. If the compensation is exaggerated, as it frequently is, there occurs the so-called inverse past-pointing which was so common in the results reported in connection with Experiment II and which is quite the reverse of what would be expected if the traditional rules for past-pointing were valid.

When the subject is commanded, either following acceleration or following retardation, to move his arms in a manner involving no external or objective reference, as in the planchette test used in Experiment III, the reflex vestibular influence upon the arm muscles is probably sensed no less keenly by the subject than in the conventional pointing test, but in the planchette test the subject feels less compulsion to compensate for this influence—with the result that the vestibular effect shows much more clearly in the overt response than when the arm movement is made with a definite objective reference. Only on the basis of such an interpretation have the writers found it possible to explain the greater consistency and greater magnitude of the deviation obtained in the planchette test than in the traditional pointing test. If this interpretation is correct, it follows that the past-pointing error should be more pronounced and more closely correlated with the direction of the preceding bodily rotation in individuals in whom either central or peripheral neural lesions exist which exclude the proprioceptive sensitivity of the arms but in whom the pointing reaction itself can still be executed. In such individuals there would presumably be no voluntary compensation and the vestibularly produced tonic disturbances would be allowed to produce their full effect on the arm movement; that is to say, in such individuals the past-pointing reaction should conform much more closely to the clinical rules than does this response in subjects with normal proprioceptive sensitivity. Likewise, in persons in whom the arm is locally anesthetized, but not paralyzed, the same situation should exist. Whether this is actually the case will have to be determined by later investigation.

SUMMARY.

This study was originally undertaken with a view to determining whether the so-called post-rotational past-pointing reaction—the direction of which is alleged, by prevailing otologic doctrine, to bear a constant and specific relation to the direction of the preceding bodily rotation in all normal subjects—is due (1) to a sensory illusion based upon vertigo or (2) to a reflex tonic imbalance produced in the musculature of the arm executing the pointing movement. It was reasoned that if explanation 1 be valid, it should be possible to abolish post-rotational past-pointing in hypnotized subjects by merely giving them suggestions calculated to suppress or eliminate vertigo. Observations made with a group of eight young adult subjects showed, however, that regardless of whether or not such suggestions were given, the post-rotational past-pointing of these hypnotized individuals was so unpredictable and inconsistent, both as regards magnitude and direction, that it was obvious that hypnotic suggestion would not afford a satisfactory technic for determining the origin of the post-rotational pointing error.

If explanation 1 be valid, i. e., if post-rotational past-pointing be due to the subject's feeling (due to vertigo) that he is moving in the direction opposite to that of the preceding actual rotation and must therefore move his arm in the *same* direction as the preceding bodily rotation in order to re-touch an object which he knows to be stationary, it follows that there should be a characteristic difference in the accuracy of the pointing reaction, depending upon whether the subject knows that the object he is trying to re-touch must rotate with him if he rotates or must remain stationary. A series of observations made with twelve normal subjects without previous rotational experience showed, first, that there was little or no consistency in the direction of the error of their post-rotational pointing when the object toward which the reaction was directed was known to be stationary (i. e., under essentially the same conditions as prevail in the clinical administration of the pointing test), and second, that when the subjects knew that the object had to rotate if they rotated, there was likewise slight consistency in the direction of the pointing error. In both cases, however, the average magnitude of the pointing error was considerably greater than the average magnitude of the so-called spontaneous error for these same subjects. These results could only be explained by assuming (a) that the majority of even so-called näive subjects recognize post-rotational vertigo as illusory and largely disregard it when executing the pointing reaction, and (b) that the vestibular stimulation arising from bodily rotation

does induce a definite tonic imbalance in the muscles of the arms, which, however, the subject senses proprioceptively and tries more or less consciously to correct for whenever the pointing reaction has *an external reference*. When this correction, or compensation, is inadequate, past-pointing occurs in the direction prescribed by the traditional clinical rules. When, however, the compensation is exaggerated, the past-pointing is in the opposite direction. This inversion of the pointing error occurs so frequently in perfectly normal subjects that it is difficult to see how the direction of the pointing error can have any diagnostic significance whatever.

If assumption (a) and (b) are correct, it follows that if, during vestibular stimulation, a subject is asked to execute a given movement of the arms which has *no objective reference*, there would be less reason for the subject's trying to compensate for the reflex vestibular effect upon the arm muscles, and this latter effect should therefore manifest itself much more clearly and consistently than when—as in the conventional pointing test—the subject is commanded to execute a response which does have an objective reference. An experiment which was designed to test this inference showed that the inference is correct and thereby lends support to the assumption from which it was deduced.

The biologic and clinical implications of the results of this study are briefly enumerated and discussed.

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IV.

PREPARING CADAVERA FOR ENDOSCOPY.

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The development of a facile technic in endoscopic procedures depends in part on cadaver practice. For the last several years we have prepared cadavera, in the Department of Anatomy of the Graduate School of Medicine, according to a technic which has proved reasonably satisfactory to the clinical demonstrators. The following is a brief report of this technic, and is presented because of the increasing number of requests for a description of our method.

Bronchoscopy and esophagoscopy can be practiced upon unembalmed cadavera as soon as rigor mortis has passed off. This has certain obvious disadvantages. Where access to suitable material is not obtainable at will, it is necessary to preserve the cadavera. In our preparation we have decided against Wickersheimer's fluid, or some similar arsenic containing fluid, because of the great tendency to a growth of mold in these preparations. The regular phenol-glycerin fluid, used for our other material, has been used for the last seven years. In this period about 150 subjects have been prepared for endoscopy. The special features of this fluid will be mentioned subsequently.

In order to have satisfactory material for endoscopy, it is necessary to select the cadavera. In our experience only about 10 per cent of the cadevera received at the anatomic laboratory make suitable endoscopic preparations. We eliminate at once those cases dying from pneumonia or tuberculosis. The hyposthenic habitus with the associated long neck is to be preferred to the short necked sthenic individual. An edentulous mouth is also to be preferred. We consider an obese cadaver not suitable.

When the material appears suitable for our purposes, all of the joints concerned—that is to say, those of the vertebral column, the shoulder, the ribs and the temporomandibular joint—are mobilized. Obviously it is necessary to wait until rigor mortis has passed off. "By steady traction each joint is once completely carried through its characteristic movements and counter movements. This produces

the maximum lengthening of the muscles acting upon the joint. This lengthening is permanent."[1]

The preserving fluid must not contain liquor formaldehyde (U.S.P.), for this produces rigidity. We use the following fluid:

Liquified phenol (U. S. P.)	15 per cent.
Glycerin (U. S. P.)	70 per cent.
Water	15 per cent.

The purpose of the water is to reduce the viscosity of the glycerin so as to permit more ready injection. For the injection we introduce, as a minimum, 16 to 20 liters of the above fluid through the right femoral artery. We have found it necessary to keep the temporomandibular joint depressed with a heavy mouth gag, due to the tendency to close which follows the filling of the pterygoid vessels with the injection fluid.

Our material commonly needs to be relieved of epithelial débris in the tracheobronchial tree by the injection and aspiration of a few ounces of water. The color of the mucosa is sometimes unsatisfactory. It is occasionally necessary to remove the upper incisor teeth. The preparations keep indefinitely if they are covered with moist cloths under oilskins. A cadaver can be used for from ten to thirty hours for practice by beginners before the parts become so displaced as to be valueless. Our material is subsequently used for dissections.

UNIVERSITY OF PENNSYLVANIA.

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V.

THE EFFECT OF RADIATION UPON CILIATED EPITHELIUM.*

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BOSTON.

INTRODUCTION.

Various theories have been advanced as to the normal physiology of ciliated epithelium and how the behavior of these cells has been altered by drugs, temperature, and the surrounding atmosphere.

Since Hilding's[1] earliest work uncovered a rich field for research, the literature has been filled with researches upon all phases of this interesting problem.

Cilia, delicate, weak, frail cilia—such is the popular conception of the type of epithelium in which we have placed a large amount of responsibility for the protection of our nasal cavities from disease. That nature is far more kind than to place a really delicate structure in direct fire of the enemy has been lost sight of by all but a few. Proetz,[2] however, early in his experiments was impressed by the hardiness of so delicate an appearing cell. It is hoped that at the conclusion of this paper, all misgivings as to the delicacy of this structure will have been lost, especially when it is realized that single massive dosages of roentgen rays as high as 24 skin erythemas† permit these cells to live.

It was at Dr. Mosher's suggestion that an attempt was made to study the effect of radium upon tissue cultures of ciliated epithelium, hoping to kill the cells at various points in their life cycle, and then by study learn something of their behavior. A number of problems arose and one or two interesting facts revealed themselves. These will be dealt with at the conclusion of this paper.

As we are dealing with another means of altering cell behavior it was thought best that an attempt be made to bring together some of the facts discovered by other workers, and to present them as a

*Read before the Academy of Otolaryngology and Ophthalmology, Cincinnati, Sept., 1935.

From the Mosher Laboratory, Massachusetts Eye and Ear Infirmary.

†Wherever the term erythemas is used, Skin Erythema Doses is implied.

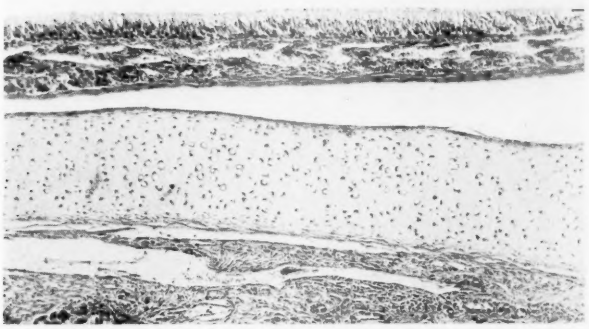

Fig. 1. This section is of the left side of the septum, opposite the side of radium implantation. The epithelium is essentially normal. The cell outlines are distinct. The nuclei are normal in appearance. The cytoplasm is clear. There are a few goblet cells but these are not excessive.

means of leading up to the main question of the paper, which is the reaction of these cells to radiation.

There will follow then a short description of the alterations in behavior produced by extraneous factors, and finally the behavior of these cells when exposed to radiation.

THE EFFECTS OF AIR CURRENTS, TEMPERATURE, AND DRUGS UPON CILIATED EPITHELIUM.

Hilding[2] was the first to conclude that this type of epithelium was changeable according to circumstances. His experiments whereby he produced goblet cells by merely closing one nostril of a rabbit are well known. With the production of stratified epithelium upon the opposite side, the side receiving the full force of inspired air, he naturally concluded that the exposed parts of the epithelium were the inactive parts, and that the protected parts were the active.

Latta and Schall,[3] in a most thorough investigation of the histology of these cells, have shown the hyperplastic potentialities of this epithelium as more protection is demanded.

The Effect of Temperature.—Proetz[5] has shown that ciliary activity is affected by temperature fluctuation. The optimum temperature is approximately 28 degrees. A temperature of 43 degrees killed the cells, whereas all ciliary motion ceased at 7 to 12 degrees C. the activity again returned at 15 degrees.

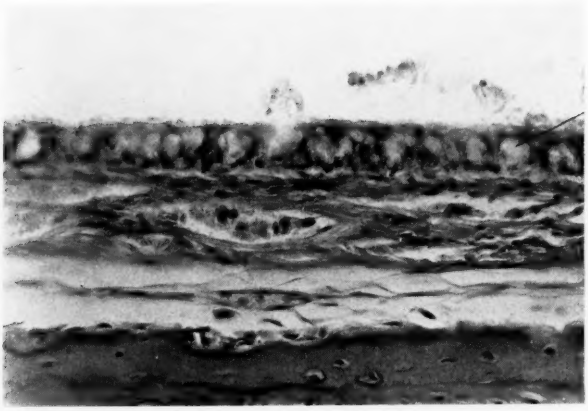

Fig. 2. This section from the same animal is from the right side of the septum. The animal was allowed to live four days following radium implantation. Note the large number of goblet cells. The cell membrane is no longer distinct, the nuclei are pycnotic, and are very indistinct, whereas the cytoplasm of the cell is a little more glandular.

Drying.—Proetz[6] found further that drying will cause cilia to cease beating, which cannot be restored after fifteen minutes.

The Effects of Solutions and Drugs.—Pursuing his researches further, Proetz[3] found that distilled water promptly produces a cloudy appearance to the cilia and the cessation of all motion, whereas solutions of sodium chloride can be increased up to five times the normal before action will cease. This action can be restored again by washing and applying normal saline.

Stark,[12] in studying irrigations of sinuses with sodium chloride noticed that the epithelial cells were larger, that their outlines were less distinct and that the cilia were rarely seen. The goblet cells appeared distended. Studying the effect of mineral oil, ephedrine oil and ephedrine inhalant on the nasal mucous membrane of rabbits, the author found that three out of ten rabbits receiving mineral oil injections showed inflammatory changes, that two out of the same number receiving ephedrine in oil showed inflammatory changes, and one out of the last group receiving ephedrine also showed inflammation. No mention was made of the effect upon the ciliated epithelium except in so far as small fat goblets were noticed in some of the cells.

Proetz[4] used tissue in situ and excised human material for the study of the effects of various drugs. His basis for studying the effect upon the cell was the vitality of the cells as measured by ciliary movement. His work has been most thorough, and for that reason

Fig. 3. This section is from the same rabbit and the side exposed to radiation, but was not as near to the radium in that it is from the inferior turbinate. Notice the very high type of epithelium and, judging from the number of cells, it would appear as if the epithelium is hyperplastic.

it is difficult to summarize and still retain all the essential features. Using ephedrine sulphate in 2 per cent and 3 per cent solutions and also in oil, he observed very little effect upon the cilia. Cocain was definitely harmful in strengths above 2.5 per cent, a 10 per cent solution causing ciliary action to cease immediately.

It has been our observation in numerous attempts to produce living cultures from nasal polyps, that if the patient was packed with cocain, no ciliary action could be observed. Frequent washings with Ringer's solution and Locke Ringer's solution failed to revive the activity.

In dilutions of 1/1000 epinephrine likewise caused cessation of the ciliary beat. Dilutions of 1/5000 and 1/10,000 caused slowing of the beat.

Camphor, menthol and thymol in 1 per cent solutions in petrolatum produced but little effect, some irritation being noted from the thymol.

Of the antiseptics, argyrol 10 per cent, mercurochrome 2 per cent, aqueous and dilutions of merthiolate 1/1000 and 1/10,000, the mercurochrome and merthiolate seem to be the most dangerous.

From these observations he concludes that ephedrine is probably not harmful; that cocain or epinephrine should be used in the weakest

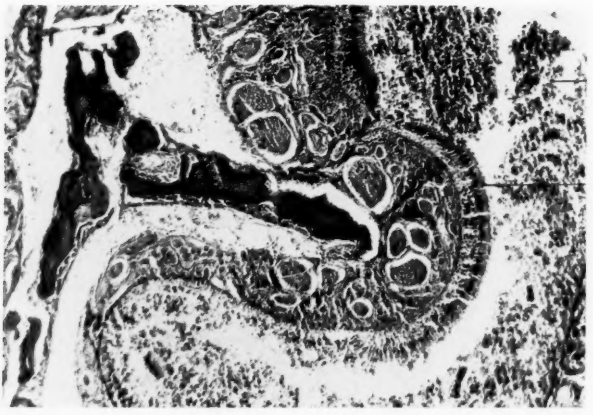

Fig. 4. This section corresponds to section III but is from the left side, the side without radium. The epithelium is hyperplastic in this case. However, considerable evidence of infection is present in this specimen, and it may be a hyperplasia for that reason.

solutions; that oily solutions should be avoided; that colloidal solutions should be avoided; that aromatics such as camphor and menthol may be satisfactory, but thymol should certainly be avoided.

Negus[13] observed the action of chloretone, glycerin and protargol upon ciliary activity. Of the three, chloretone one-half per cent causes paralysis, glycerine 5 per cent produces a retarding effect, protargol in 1 per cent solution produces no harmful effect.

The same author studied the effect of anesthetic vapors and concluded that carbon dioxide and chloroform have but little effect upon the activity of the cilia.

Lierle[14] and Moore in further studies have shown that a 2 per cent zinc sulphate and a one-half per cent silver nitrate solution are detrimental to ciliary activity, permanent cessation of activity resulting from the application of the latter drug.

It is difficult to summarize the results of the numerous researches just quoted. Clinical applications can undoubtedly be advanced. However, condemnation of a drug because it shows the activity of the cilia is certainly unwise, for ciliary activity seems to be about the only yardstick that we possess when it becomes necessary to study the effects of various environmental influences upon ciliated epithelium. Suffice it to say that as long as this holds true it would seem that any drug producing a marked defect in that activity should be used with caution.

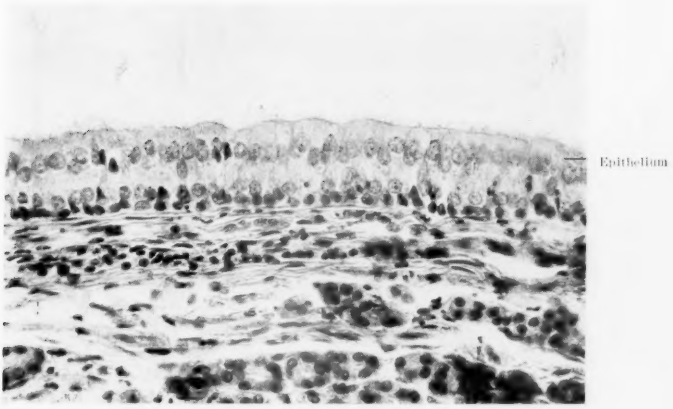

Fig. 5. This is from the unradiated side of the second rabbit living fifteen days following radium implantation. It is a beautiful example of normal ciliated epithelium from the septum. Cell outlines are distinct, the nuclei are normal, and no hyperplastic changes are noted.

OBSERVATIONS UPON LIVING CILIATED EPITHELIUM FOLLOWING EXPOSURE TO RADIUM AND X-RAY.

Every once in a while during the course of investigation, in some particular field, the original line of thought is interrupted and in its place is substituted some other problem born of interesting observations, while attempting to carry out the primary problem.

The original intention in this case was to study the action of radium upon tissue cultures. However, in the light of subsequent developments the word "cultures" has been dropped and the words "living ciliated epithelium" used. In other words, the following observations are made upon living cells and not the growth of these cells.

Method.

The observations are in reality upon three different types of experiments. These three will be mentioned and the methods used in each case outlined.

Since it was always available, Dr. Mosher suggested the use of tracheal tissue from rabbits. This organ furnished most of the ciliated epithelium except in one case, in the experiment where the cilia beat for eight days. That epithelium was removed from a nasal polyp. Though rigid adherence to sterile technic was not in force, all instruments, glassware and solutions were sterilized.

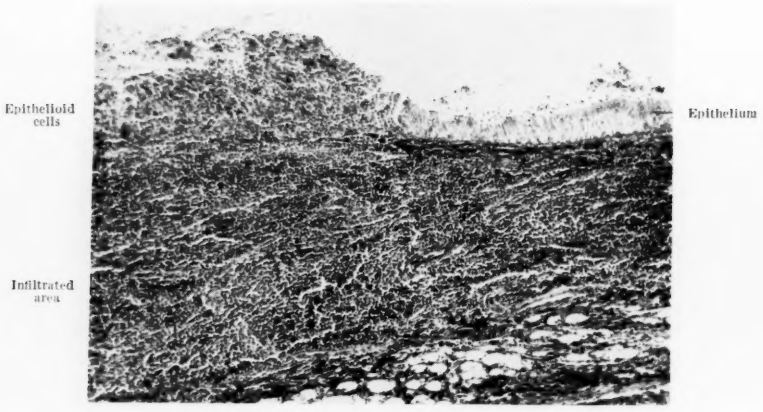

Fig. 6. This is from the radiated side of the rabbit. In this section there is a hyperplasia of the epithelium about an area where the epithelium seems to have been destroyed. Close observation reveals many epithelioid cells, but no order of arrangement and no cellular outline. There is a dense infiltration of lymphocytes.

Pieces of tracheal tissue, one-half mm. in size, were removed and placed in a hanging drop. One mount was used as a control and one was exposed to radium. The tissue was incubated at 28 C. Radon seeds of 1 mc. each were used. These were placed over the cover glass in a circle and were never any more than .5 cm. away from the tissue. The cover glass did not contain lead. The seeds were left in place until the death of the tissue.

The following observations were made:

Shortly after the placing of 6 mc. seeds about the tissue ciliary motion increased. Thereafter it seemed that an increase in ciliary activity was evident with the placing of every dose.

With constant exposure to 6 mc. the tissue lived ninety-six hours. The control lived eight days. Nothing startling was observed, though the growth in both cases seemed to be from the basal layers.

Thirteen attempts at varying the total dosage were tried. However, it soon became apparent that the results were very inconsistent. About the only observation that was made was that very little effect was noted from the radiation. It was then thought that by using x-ray the following factors could be controlled.

1. The dosage could be accurate.

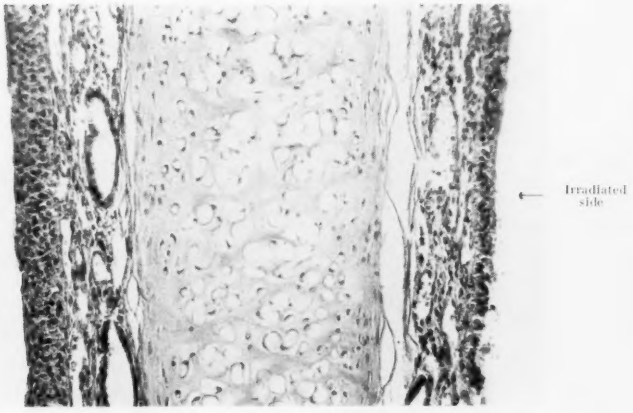

Fig. 7. This section shows both sides of the septum. The animal was allowed to live two months following irradiation. The side opposite the radium shows stratified squamous epithelium, whereas the side of irradiation shows destruction of the epithelium down to the basal layer.

2. The tissue could be exposed directly to the action of the ray.

3. Very high dosage could be obtained.

The following plan of using x-ray was adopted:

After removal of the trachea from the rabbit it was cut into equal portions and each portion washed thoroughly. One specimen was placed in a test tube containing Ringer's solution. The other was laid upon a piece of sterile gauze and kept moist by means of slowly dropping Ringer's solution. This specimen was exposed to the roentgen ray. The rays were not filtered and the target skin distance was eight inches. In all cases single exposures were employed, the machine running at 100 K.V. and 5 M. A.

Following radiation, a small piece of the mucous membrane was removed and placed in the hanging drop. The rest of the tissue was placed in a test tube containing Ringer's solution and kept at a temperature of 14 C. The same was done with the control. From time to time as the hanging drop specimens died, new specimens were made by using the specimens kept at 14 C.

Dosages were started at 4 skin erythema doses, and will be reported in the order of experimentation.

The tissue receiving four S. E. D. lived 120 hours, the control dying at the same time. No visible effects on the ciliated cells were noted, including observations upon the rate of the ciliary beat.

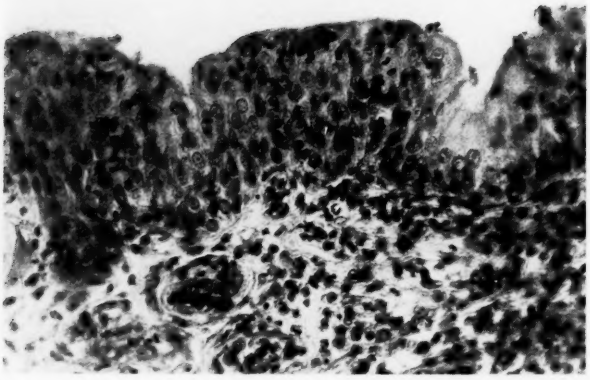

Fig. 8. High power of section of rabbit's nasal mucosa removed from the septum two months following irradiation. The epithelium is markedly hyperplastic. Some degree of its activity may be obtained by the number of mitotic figures present.

Eight erythemas (2800 r).

The tissue lived 168 hours.

The control lived only 48 hours.

Sixteen erythemas (5600 r).

The tissue lived 168 hours.

The control lived 144 hours.

It was thought that at the end of 120 hours, those specimens having received x-ray were a little more active, as measured by the rate and force of the ciliary beat.

Twenty-four erythemas (8400 r).

The specimens which received x-ray lived 314 hours; the control living but 216 hours.

It was observed that after 120 hours, the tissue having received the radiation seemed a little more active and that the amount of débris in the surrounding medium was less than that of the control. By débris is meant dead cells for the most part and leucocytes.

At this point the question arose as to whether or not the metabolism of these cells was being affected. It was decided that some idea of the metabolic rate might be obtained by determining the P.H. of the solutions containing the tissue.

Therefore the experiment of using 24 erythema doses was repeated. This time the exposed tissue lived 168 hours and the control lived 96 hours.

Repeated again, the tissue receiving the radiation lived 192 hours and the control 188 hours.

The P.H. determinations were run up on all solutions and showed so much variation that they were discounted as valueless.

Following this all pyrex glassware was used, the solutions were pipetted and extra controls adopted.

The results were as follows:

Tissue I received 16 erythema doses; lived 192 hours. P.H. of solution 6.2.

Control lived 192 hours. P.H. 6.0.

P.H. of Locke Ringer's solution 7.3.

P.H. of solution subjected to same temperature and conditions as those containing tissue 6.6.

Tissue II received 24 erythema doses; lived 192 hours.
P.H. of solution 6.0.
The control lived 192 hours and had a P.H. of 6.00.
Locke Ringer's solution had a P.H. of 7.3.
The control solution a P.H. of 6.4.

The dosage was now increased to 32 erythemas or 11,200 r. Three sets of tissue were exposed to this increased dosage.

Tissue No. I.

The irradiated tissue lived 48 hours.
The P.H. of the solution was 6.0.
The control lived 96 hours. The P.H. of the solution was 6.0.
The P.H. of Locke Ringer's solution was 6.9.
The control solution had a P.H. of 6.4.

Tissue No. II.

The irradiated tissue lived 96 hours.
The P.H. of the solution was 6.00.
The control lived 168 hours.
The P.H. of the solution was 6.00.
The Locke Ringer's solution had a P.H. of 6.6.
The control solution had a P.H. of 6.3.

Tissue No. III.

The irradiated tissue lived 48 hours.
The P.H. of the solution was 6.00.
The control lived 72 hours.
The P.H. of that solution was 6.00.
The control solution had a P.H. of 6.4.

In general the solutions containing the irradiated tissue and the control had a P.H. of 6.0, the fresh Locke Ringer's solution a P.H. of 7.3 and the control solutions a P.H. of 6.4.

It would seem as if the variation between the control specimens and the irradiated tissues was not enough for any conclusion as to acceleration or retardation of metabolism.

Of considerable interest is the viability of the tissues subjected to the increased dosage of 32 erythemas. The three tissues exposed to this dosage lived 48, 96 and 48 hours, respectively. The controls lived 96, 168 and 72 hours.

From these results it would appear as if an x-ray dosage of 11,200 r was required before any gross effect upon the viability of the ciliated epithelium could be noticed. For the first time during the course of the experiments the control tissue lived longer than the irradiated tissue. In this respect it is of interest to quote the following from Dr. Fenton's[17] paper. "Study of tissues from infected antrum mucosa and cyst walls from a man of 36 who had received doses of deep roentgen rays (because of suspected malignancy) showed enormous thickening and fibrosis of the tunica propria, many plasma cells, and almost normal epithelium."

The third portion of the paper deals with the actual implantation of radon seeds in the nostrils of rabbits. The procedure was carried out along the plan suggested by Dr. Mosher. The same number of seeds was used in each case, the variable being the length of time the animal was allowed to live following exposure.

Five 1 mc. seeds were used. The seeds were partially imbedded in a small mould of dental compound and then inserted in the nostril. The mould was then secured by means of a suture partially closing the nostril. At the end of three days the sutures were removed. In some cases they had sloughed out. It was hoped that in this manner a rather superficial dosage was acquired and that the length of time the nostril was closed would not be sufficient to produce the changes noted by Hilding![2]

Section I.

This section is of the left side of the septum, opposite the side of radium implantation.

The epithelium is essentially normal. The cell outlines are distinct. The nuclei are normal in appearance. The cytoplasm is clear. There are a few goblet cells but these are not excessive.

Section II.

This section from the same animal is from the right side of the septum. The animal was allowed to live four days following radium implantation. Note the large number of goblet cells. The cell membrane is no longer distinct, the nuclei are pycnotic and are very indistinct, whereas the cytoplasm of the cell is a little more granular. This section illustrates what I believe to be the early changes resulting from radiation.

Section III.

This section is from the same rabbit and the side exposed to radiation, but was not as near to the radium in that it is from the inferior turbinate. Notice the very high type of epithelium and, judging from the number of cells, it would appear as if the epithelium is hyperplastic. If so, this type of epithelium would correspond somewhat to the type described by Latta and Schall[8] as being hyperplastic as a means of furthering protection.

Section IV.

This section corresponds to section III but is from the left side, the side without radium. The epithelium is hyperplastic in this case. However, considerable evidence of infection is present in this specimen, and it may be a hyperplasia for that reason. It is unfortunate in that we cannot say that radium produces epithelial hyperplasia as compared to the opposite side. However, the suggestion is certainly present.

Section V.

This is from the unradiated side of the second rabbit living fifteen days following radium implantation. It is a beautiful example of normal ciliated epithelium from the septum. Cell outlines are distinct, the nuclei are normal, and no hyperplastic changes are noted.

Section VI.

This is from the irradiated side of the rabbit. In this section there is a hyperplasia of the epithelium about an area where the epithelium seems to have been destroyed. Close observation reveals many epithelioid cells, but no order of arrangement and no cellular outline. There is a dense infiltration of lymphocytes.

Section VII.

This section shows both sides of the septum. The animal was allowed to live two months following irradiation. The side opposite

the radium shows stratified squamous epithelium, whereas the side of irradiation shows destruction of the epithelium down to the basal layer. It is quite probable that the radium has made its effect manifest upon the side showing the stratified epithelium, as well as the side devoid of epithelium. Consequently, that side has undergone hyperplastic changes to the point of an absolute change in morphology, whereas the side receiving the full dose of radium has passed through this stage and has entered the stage of destruction.

Section VIII.

This section is from another rabbit allowed to live two months following irradiation. The large number of mitotic figures is an index of the type of activity the epithelium is undergoing.

From these studies it would appear as if ciliated epithelium undergoes the following changes following radiation:

1. Hyperplasia.
2. Loss of cell outline and the production of pycnotic nuclei.
3. Goblet cell formation.
4. Destruction down to the basal layer.

The minute cellular changes produced by x-ray have been thoroughly studied and published in a volume by Colwell.[16] These studies are concerned with types of tissue other than ciliated epithelium.

For the sake of completeness, we are attempting studies upon the mitochondria and Golgi network in ciliated epithelium following exposure to x-ray.

The functions of these two cytoplasmic inclusions are still not definitely known. Many workers, however, contend that the mitochondria have to do with respiration. Therefore, the possibilities of research along this line are rather exciting.

Briefly, we are using a supervital stain of Janus Green B for the mitochondria. The other procedures for fixed specimens are the Bensley-Altman method for mitochondria and DaFano's modification of Cajal's silver impregnation for the Golgi apparatus.

Under supervital staining it would appear as if x-ray produces a clumping and then a vacuolization of the mitochondria, though this observation is awaiting confirmation by the study of fixed specimens.

The work has just been started and no definite conclusions are to be drawn from this stage.

SUMMARY.

The foregoing paper is in two parts. The first deals with some of the outstanding contributions to the literature within the last five years, pertaining to the effects of drugs upon ciliated epithelium.

The second part has recorded observations made upon the behavior of ciliated epithelium after exposure to radiation. Three methods of approach to this problem were used: namely, the exposure of hanging drop specimens of ciliated epithelium to the action of radon seeds; second, the exposure of sections of rabbit's trachea to the direct action of roentgen ray; third, the implantation of a fixed dosage of radium in the nostrils of rabbits and observations upon the histologic specimens made at varying lengths of time after the implantation.

CONCLUSIONS.

1. Goblet cells may be another form of ciliated epithelial cells. Furthermore, they are probably degenerative, as shown by changes noted in the nasal mucosa of rabbits after exposure to radium.

2. The metabolic rate of the cells evidently was not affected by roentgen ray when this metabolic rate was measured by changes in the P.H. of the solutions containing the tissues.

3. It may be possible that some dosages of roentgen ray are actually stimulating. Therefore, there should be a dosage that will produce beneficial results.

4. Ciliated epithelium is not a delicate structure. If one considers that a single dose of unfiltered roentgen ray of eight erythemas is the maximum for the skin of man, the picture of the severity of a burn produced by a single dose three times that amount, or twenty-four erythemas, is almost beyond one's imagination. However, the evidence points toward the fact that these frail appearing cells do stand such a dosage with impunity.

In searching for an answer to the question, "Why are these cells so remarkably viable?" I can find no better explanation than the one offered by Dr. Werner Mueller, namely, that cilia are an ancient structure biologically; that, therefore, in the order of events, they should be the last to be destroyed.

The author wishes to express his sincere thanks to Dr. G. H. Holmes and his staff of the X-ray Department at the Massachusetts General Hospital for the use of their x-ray equipment and radon seeds necessary for the carrying out of these experiments; likewise for such technical advice as was essential for their use. The photomicrographs were taken by Dr. Werner Mueller.

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VI.

A NEW MASTOIDECTOMY INCISION AND WOUND CLOSURE.*

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Since Schwartz first described the technic of a mastoidectomy, in 1873,[1] there has been very little departure in the type of operation. Various drugs have been used to promote wound healing, but even the attempt has been a pathetic indication of the lack of understanding of the physiology of wound repair.

It was not until I had labored rather diligently for three years in the experimental laboratory that I learned quite thoroughly that my sincere attempts to induce wound healing had often acted inversely proportional to the application of my labors.[2]

In 1928 I described an irritation phenomenon of the dura[3] with the use of gauze packing in the mastoid wound, and upon two occasions I have seen thrombophlebitis of the sigmoid sinus develop subsequent to its surgical exposure and the irritation and necrosis of the exposed vessel wall in the presence of wound infections.

Gauze is a foreign body and all wounds react to it as such. It is irritating, nonabsorbable and delays normal wound healing. Its presence predisposes to infection, and when infection is present gauze promotes its activity.

TECHNIC OF PROCEDURE.

For the past two years I have been closing the mastoidectomy wound completely, at the time of the operation. During that time I have had very little difficulty with this radical departure from past methods of postoperative care of the mastoid wound.

There are certain departures in the operative technic which play an important part in the success of this procedure. The postauricular incision should parallel the posterior border of the external ear when it is held flat against the side of the head. (Fig. 3.) This carries the incision well up above the external ear, along the zygoma and back

*From the Department of Experimental Medicine, University of Kansas.

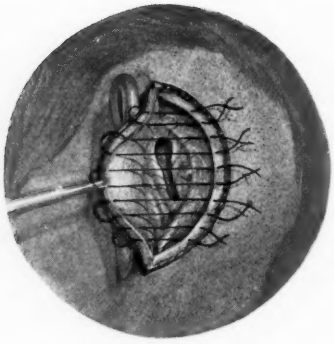

Fig. 1. Shows the periosteal flap held forward, exposing the completely dissected mastoid cavity with the facial ridge lowered, the antrum widely open, and the bone edges sloping evenly into this cavity. There is a small area of exposed sigmoid sinus. The periosteal mattress sutures of absorbable catgut are in place, preparatory to tight closure.

Fig. 2. This shows the overlying deep skin mattress sutures which tightly close the wound and fix the periosteum and the overlying soft tissues back into their former place.

Fig. 3. Shows the mastoidectomy wound with the skin sutures removed five days postoperative. This scar rapidly diminished, is covered by hair, and there is no postauricular depression. Having been placed farther back in the scalp, the rich blood supply promotes prompt healing.

into the border of the hair line, which brings it along the posterior edge of the mastoid process. The incision should be carried down through the periosteum to the bone, and the periosteum should be elevated, along with the flap, and should not be torn or traumatized. (See Fig. 1.) By placing the incision in the scalp the blood supply is greatly increased and the well known rapid scalp healing follows.

While operating, this flap should be covered with warm, moist sponges. After the mastoid dissection is completed the facial ridge should be lowered and the zygomatic angles smoothed off, so that no sharp overhanging bone edges are left to press upon this overlying periosteal flap. All spicules of bone should be carefully removed from the wound, and any accumulation of blood or serum should be thoroughly cleaned out.

The periosteum is then sutured back to its original position by absorbable mattress sutures (Fig. 2) and replaced, as nearly as possible in its original position. Just prior to the insertion of the lower suture the flap should be firmly massaged from the antrum downward, in order to exclude any blood or serum which has accumulated during this stage of the operation.

There is no contraindication, however, in covering the exposed sigmoid and dura with this flap, as it is an imitation of nature's method of protection.

A soft roll of cotton or a small sea sponge is then moulded to this postauricular area. While the assistant firmly presses the periosteal

flap in position the external ear is covered with vaselin, soft cotton and flat gauze, and the mastoid wound is firmly bandaged in the usual manner. Cotton should be applied directly over the external ear, because gauze may cause pressure necrosis and is usually painful.

These dressings should not be disturbed for four days, and care should be taken not to move the external ear, because it might elevate the newly adhered flap. With the antrum freely opened, sufficient drainage is established through this route by way of the external auditory canal.

If suppuration does occur within the wound, no time has been lost, as a suture can be removed and drainage established at the lower angle.

EXPERIMENTAL EVIDENCE.

In order to be more thoroughly convinced that the periosteal flap closure was a sound surgical principle, various experiments were carried out upon the dog.

Under amytal anesthesia, trephine openings were made just away from the midline of the anterior portion of the skull. The periosteum muscle and skin attachment over the anterior portion of the skull was elevated. The underlying bony skull was removed and the periosteum replaced. Later examinations and x-ray studies proved that bone regeneration took place in direct relation to the periosteal replacement.

I later discovered that Macewen[1] had proved the same principle in his experiments and illustrates the importance of the periosteum in bone wound healing by its definition as a "fibrous membrane, composed of two layers, the inner of which 'contains many elastic fibers and blood vessels in a minute state of subdivision.' Between the inner layer of the periosteum and the bone is a quantity of areolar tissue which is admirably adapted for cell growth. Its loose attachment permits easy penetration of the osteoblasts emanating from the underlying osseous tissue. Its rich blood supply nurtures and lymph supply encourages this rapid proliferation."

Experiments upon the dog showed that replaced periosteum retards infection of the wound and hastens bone regeneration.

The patient is extremely grateful for the escape from pain which accompanies the removal of the gauze packing, and the boresome annoyance of repeated postmastoid dressings is avoided. There is less scar formation, as only a slight depression is left (see Fig. 3), and a

much better exposure of the operative field is made by this incision. The ordinary mastoid spreading retractors are unnecessary, and when a considerable area of the dura of the middle cranial fossa is exposed this is much the better way to promote prompt healing.

Chronic fistulous tracts may also be closed by this method where secondary operations are necessary, and I have obtained some very remarkable results in operations upon cholesteatomas that have not been watched long enough to bear reporting.

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VII.

ALLERGY OF THE UPPER AIR PASSAGES: INHERITED AND ACQUIRED FACTORS.*

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Some of the recognized allergic disorders in order of importance, as concerning the ear, nose and throat men, may be mentioned as follows:

1. Vasomotor rhinitis (allergic coryza).
2. Asthma.
   Eczema; urticaria; angioneurotic edema;
   Erythema multiforme.
   Dermatitis venenata.
3. Migraine.
4. Vernal conjunctivitis.

The history of allergy is not without its romantic side. It dates back thousands of years and references can be found in early writings of the Talmud. As we peruse the pages of medical history we are amazed at the dark superstition in which the subject had been submerged. It is heartening, however, to note that the gradual evolution of thought on allergy, as we understand it today, has painfully emerged from the abyss of ignorance, sorcery and witchcraft, and today commands attention as the most subtle fields in specialized medicine.

The word allergy means altered reactivity of the individual. It was introduced by von Pirquet and for want of a better description it has become a fixed term in immunology. Its usage is interchanged with hypersensitiveness. Richet with Portier in 1902 reported their observations in dogs. Arthus described the well known reaction in rabbits which takes the name of the Arthus phenomenon. Theobald Smith reported his observations on hypersensitiveness to horse serum in guinea pigs.

In Germany, Anderson and Rosenow spoke of it as "Reaktionenfähigkeit," so when we speak of anyone having allergy to chemicals,

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foods or drugs, it conjures to the mind an altered reaction of the individual.

One clear cut definition of allergy is a "changed capacity to react to foreign substances." When the symptom-complex fulfills certain criteria, they may be considered allergic in origin. These criteria are: (a) The symptoms must be produced by contact with a particular agent, foreign to the body; (b) the symptoms must disappear when this contact is interrupted; (c) the demonstration by skin tests of the patient's specific hypersensitiveness.

For the lower animals, the coined term anaphylaxis is used, which means without protection as contrasted with prophylaxis. The term anaphylaxis has been subjected to considerable criticism, but the fundamentals, as proposed by H. G. Wells,[1] stand today irrefutably.

1. When an animal, for example the guinea pig, is hypersensitized with a foreign substance, the peculiar reactions cannot be reproduced in a nonsensitized animal. That is to say, specific toxin applied to specific animal tissues will produce specific changes, for which we have the classical experiment of Schultz and Dale in the realm of animal experimentation, e. g., by removing the uterus of the sensitized guinea pig and suspending it in a bath of Locke's solution. When the antigen was added to the bath fluid, the uterine muscle showed immediate contraction followed by relaxation.

2. The symptomatology does not vary as long as that specific antigen is used in the same quantity, but will vary when another species of animal is introduced.

3. When the blood of a sensitized animal is transferred to another animal of the same species, passive anaphylaxis is brought about. The first animal represents the active anaphylaxis, and the second animal the state of passive anaphylaxis.

4. In the event that we precipitate shock or bronchospasm, we should be able to control this pathologic change with atropin or epinephrine.

5. Finally, after the animal recovers from shock, he should enter into the stage of desensitization, commonly known as anti-anaphylaxis.

In 1903, Arthus,[2] while experimenting with rabbits, described a local phenomenon which bears his name and is called the Arthus phenomenon, which is seen when a specific protein is injected sub-

cutaneously. At that site a swelling occurs with edema and necrosis of the tissue. It is a purely local reaction and I could call this regional anaphylaxis. In this connection may I cite the case reported in the Journal of the American Medical Association,[3] of a boy 4½ years of age who had received an injection for diphtheria toxin-antitoxin the year before, for immunization purposes, and one year later he received a scalp injury. He was given tetanus antitoxin, which resulted in marked sloughing of the skin at the site of the tetanus injection, with marked septicemia and death supervening. A patient of mine, about 56 years of age, developed marked suppuration of the free edge of the soft palate. I diagnosed this as Arthus phenomenon, since this condition followed novocain injection for the extraction of a molar tooth.

Doerr[1] gave us a very simple classification of anaphylaxis. He divided it into four categories: (1) Active sensitization; (2) Passive sensitization; (3) Desensitization, and (4) Local sensitization, or Arthus phenomenon.

To reduce these technicalities in terms of human experiences such as we sense in the world of romance, it may be said when a young man is strongly attracted to his mate, we can say he is being subjected to "active sensitization," a form of hypersensitive romanticism. If he happens to marry her, this attraction can be readily transferred to other members of the family or his friends; then we have brought about passive sensitization. If, through some unforeseen circumstances, this beautiful romance goes on the proverbial rocks, where disillusion and dissolution of the marriage must take place, then the process of desensitization begins. I need not amplify this any further.

Active anaphylactic sensitization is established when the anaphylactogen is introduced, resulting in the production of antibodies in a hypersensitive state. The avenues of approach may be intraocular, intravenous, intraperitoneal, subdural or subcutaneous.

The reticulo-endothelial system plays a definite part in the production of immune bodies. We know that colloidal substances, when injected intravenously or intraperitoneally into animals, are immediately taken up by the endothelial cells. The greatest amount of the substances are taken up by the liver, spleen, lungs, lymph nodes and bone marrow.

Metchnikoff[5] belived that the antibodies are formed as the result of the ability of the phagocytic cells to ingest and digest foreign materials and that the seat of formation was the reticulo-endothelial

system. This has led investigators to saturate or block the cells of the reticulo-endothelial system by injection of particulate materials or colloidal dyes, then test their ability to form antibodies.

Desensitization.—Besredka and Steinhart[6] referred to it as anti-anaphylaxis and called it a condition in which the animal no longer reacts to the same protein or serum injection.

Atopy.—Coca coined this word to explain hypersensitiveness conforming to hereditary laws. He called the serum atopic reagins and is of the opinion that they have a distinct familial tendency. Ella Grove tried to establish a relationship between man and monkeys by experimenting with monkeys of the ring-tail variety, as well as the chimpanzee. She attempted to bring about local sensitization from man to monkeys with the method of Prausnitz and Küstner, and then by inducing a constitutional reaction by the reinjection of a suitable extract of sensitizing human serum. While these experiments were negative, the chimpanzee was the only animal showing some sort of a reaction.[7]

Living matter is extremely complex, making the study of vital phenomena in living animal tissue exceptionally difficult. There are obstacles to overcome when studying immunologic chemistry in vitro as compared with in vivo, for the reaction in the test tube differs from the reaction in living tissue. Through these manifestations of physical and chemical energy which underlie the interaction of colloid matter, our conception of the immune processes has been greatly developed. Wadsworth and Wheeler,[8] in 1928, produced a potent diphtheria toxin in a synthetic medium. They demonstrated that a potent toxin could be produced only when the calcium, phosphate and peptone were combined in a colloidal state. It has been shown that in the combination of acid and base certain adsorption phenomena takes place and that these, as well as a definite hydrogen-ion concentration are essential. Landsteiner and Jagic[9] have advanced the colloidal absorption theory.

Loeb[10] and others found that sodium, potassium and calcium were essential in the regulation of such reactions as stimulation, irritability, inhibition and similar phenomena. If the process of stimulation is based upon an exchange of ions and the functional effect of this upon their proportions and dissociation in the tissues, Loeb concluded that the substitution of one ion for another alters the physical properties of the protein compound and that these changes are essential properties of living matter. There is a development of immunologic specificity apparently depending upon a development of chemi-

cal individuality of the protein. This has been emphasized by Landsteiner,[11] Wells[12] and others. Of course, Walbum and Mörch[13] showed that electrolytes can influence the development of such an immunochemical or physico-chemical system in the use of manganese chloride which causes a stimulation of antibodies. Castelli[14] showed a definite drop in calcium following toxemia in animals. There is a relation between the calcium and the protein content of the serum. It is a well known fact that horses undergoing intensive immunization against bacterial toxins show a considerable increase in the serum globulins, and it might easily be expected that there would be an accompanying disturbance of the calcium equilibrium. On the basis of the experimental data obtained in a study of serum from horses undergoing immunization with diphtheria toxin, the diffusible calcium in the serum displayed a noticeable tendency to decrease in the twenty-four hour period following the injection of large amounts of toxin. A somewhat similar tendency was also noted in the case of the total calcium and the total base. There was considerable fluctuation in the amounts of total and diffusible phosphorus during the immunization period, but with no apparent relationship to the development of immunity, although these values tended to decrease as the antitoxic potency increased. It is suggested that this drop in diffusible calcium, and possibly also in other electrolytes, is a chemical factor related to the immunologic stimulation process.

Dunbar[15] advanced the idea that the immunologic property is of a protein nature and is linked with the carbohydrate molecule. Wells and Osborne,[16] White and Avery[17] and Lake, Wells and Osborne[18] stated that specificity of anaphylactic reaction depended upon the complex chemical structure of the protein molecule, practically agreeing with the idea. This led Vaughan to call this chemistry protein poisoning, which produced a bacterial toxemia also called "anaphylatoxin." As the name implies, this is a toxic substance or a split product of bacterial origin and is formed whenever bacteria and active conditions meet. We do know that when antigen and antibody meet, poison is produced and this may give rise to systemic reactions in the body of animals and man. Friedberger called this substance anaphylactogen. It is obvious that experimental analysis such as we observe in animals bears a strong resemblance to the chemical changes in the blood of the human individual. Man may become hypersensitive to such proteins as egg white, chemicals or drugs which enter the system, are absorbed and broken down into more simple chemical structures in the body. The active principle may be sero-albumin, sero-globulin, proteases or alcoholic extract. These proteins may con-

tain a chemical complex which is responsible for its specificity. This is found in egg white, horse dander or ragweed pollen.

We know of instances in which an infant or a child who is allergic, develops an acute middle ear condition, complicated mastoiditis and that conditions improve when the offending food article, such as egg or milk, is removed from the diet. Many of these cases have been unnecessarily exposed to the danger of a surgical procedure when a little knowledge of food allergy would have forestalled a tragedy.

Mechanism of Allergy.—Of all the allergies, the one holding our attention is the bacterial form of hypersensitiveness resulting from a bacterial or infectious process. Zinsser and Parker[19] took anti-typhoid serum from a rabbit and were able to sensitize the uterus of a young guinea pig, according to the Dale method, by producing a typical contraction. In bacterial hypersensitiveness there is always a delay in bringing about the reaction. The antibodies are in the cells.

In speaking of allergy we are concerned with the susceptibility of some persons to these protein products. The question is asked as to what substance brings about these reactions, and the answer is that the formation of antibodies is responsible for the reaction, whether it occurs in lower animals or in man. When the antigen comes in contact with the cells an intense reaction takes place, resulting in a concentration of antibodies which can be demonstrated in the serum of the patient. These antibodies gradually disappear when the patient is on the road to recovery.

Prausnitz and Küstner (1921) showed that the serum of a patient sensitive to egg (Prausnitz) can be transferred to another patient sensitive to fish (Küstner). The allergens are agents which are usually of protein origin, or protein derivatives which are responsible for the sensitization process. Allergens can be found in sera, foods, dandruff and drugs.

The allergens which are free from fats cannot produce sensitization. In plant life these allergens may be linked to the carbohydrate molecule. When these allergens gain access to the body through inhalation, they are called (a) inhalants, (b) ingestants when they find their way in through food, (c) contactants when they come in contact with the skin, and (d) injectants when the foreign body is introduced via the hypodermic needle. These allergens when they enter the system bring about the formation of antibodies. Antibodies may be free in the blood serum, such as found

in hay fever, asthma and some cases of eczema. The Prausnitz-Küstner reaction has been able to demonstrate the presence of antibodies in the blood. In other words, these allergens or antibodies can be demonstrated in patients suffering from hay fever or asthma.

Two Mechanical Theories.—Out of a welter of theories, such as the fermentative and digestive theories, it has now finally been narrowed down to two schools of thought. Dale and his associates[20] have been able to demonstrate the presence of histamine in the unstriped muscle as the cause of anaphylactic shock.[12] Thomas Lewis[22] was able to produce a wheal on the human skin which confirmed Dale's findings. In the cellular theory we have the suggestion of colloidal equilibrium with a change in the surface tension of the blood, causing precipitation of the endothelial cells which brings about shock.

The theory of Lewis may briefly be expressed as follows: "The interaction of antigen and antibody in susceptible tissues brings about a liberation of the loosely combined histamine normally present in the tissues, and it is the liberated histamine which causes the ultimate physiologic effect known as anaphylactic shock or the atopic reaction, as the case may be: the theory is thus not incompatible with the well established cellular theory of hypersensitiveness." Opposed to this thought is Doerr supporting the humoral theory. Investigators have repeatedly shown, through the process of experimentation, that anaphylactic shock in the chemical world represents a dispersion of colloids through the organism. The clinical picture of the symptoms and the anatomic changes underlying anaphylaxis are nearly identical in all animals.

Shock may take place by the introduction in the animal of the serum of another animal already immunized, which is passive anaphylaxis. Or the introduction of toxic serums of other animals, such as immune serum, extracts of organs, substances of vegetable or animal origin. Kritchevsky and Birger[23] referred to it as a "shock of metaballo-dispersion." Then the issue arose as to whether anaphylactic shock took place in the blood or in the cell of the organism, and the two differing followers have sprung up.

First, we have the humoral theory adherents, led by Vaughan, Friedemann, Friedberger and De Waele. These gentlemen are of the opinion that anaphylactic shock takes place in the body fluids. Besredka, however, was among the first to initiate the thought that shock takes place in the cellular tissues, hence the name, the cellular theory. However, it was left to Dale and his classical experiment to give credence to the histogenic theory of anaphylactic shock.

"Uteri of normal and sensitized virgin guinea pigs were cut out, having preliminarily been freed from blood by washing out through the aorta abdominalis. They were then immersed in 250 cc. of Ringer's solution, and then subjected to the action of the serums, the contractions being recorded by a miograph. Dale found that the uterus of a guinea pig, actively or passively sensitized to horse serum, reacts by contraction immediately after 0.1, 0.025, and even 0.0025 cc. of horse serum are introduced into the vessel containing the 250 cc. of Ringer's solution, while a normal uterus does not contract, even if the solution in which it is immersed contains 1 cc. of this antigen."

In the same manner it has been shown[24] that the protective rôle in anaphylactic shock is not only participated in by the colloids in the blood but also by the colloids in the tissues and cells of the organism. The connective tissue takes upon itself the defense of those organs which are more essential for health and the preservation of life. Schultz, Dale, Manwaring and Coca with their experiments represent one solid phalanx to the critics of the cellular theory. The guinea pig and dog give us the irrefutable evidence of the cellular theory in which perfusion plays a most important part.[25 26 27]

Hereditary Influences.—There is an overwhelming evidence that the transfer of specific blood from the mother to the offspring takes place through the placenta. In the case of rabbits, guinea pigs, cats and man antibodies have been found to reach the fetus through the placenta. Mammary secretion also plays a dominant rôle in transmitting and spreading these antibodies among animals of the higher order.

Ratner[28] indicates that the respiratory mucosa may serve as a site for the spontaneous introduction of the antigen which may reach and sensitize the fetus in utero. According to Holford,[29] horse hemoglobin has not been found to pass the rabbit placenta, whereas egg albumin, horse or beef serum injected into pregnant rabbits near term has been found in a number of instances to pass the placental barrier in quantity sufficient for demonstration in the serum of the fetus.

H. and L. Hirszfeld and Brokman[30] recently studied the relation of diphtheria susceptibility with reference to the inheritance of the blood groups. By paying particular attention to the susceptibility of diphtheria, they were interested to find that the so-called natural immunity to diphtheria takes place only after contact with the diphtheria bacillus and affords evidence that the capacity of that antitoxin production in human beings is inherited. According to the Hirszfelds and Brokman, if both parents are susceptible, that is, the

Schick test is positive, the children would be likewise susceptible, and when the parents are immune the children would show a certain amount of immunity. In other words, immunity, according to the Hirszfelds and Brokman, could be inherited. However, Philip Levine[31] disagrees with the findings of the Hirszfelds and Brokman. In an exhaustive study he could not find any data which would support the evidence that an atopic hypersensitiveness is inherited.

Persons who suffer from atopy, particularly the hay fever type, have been known to show a hereditary tendency. The observers, on the basis of clinical and experimental evidence, have called those sites "atopic tissue" or "shock organs," and they have found that the nasal mucous membranes, the bronchial wall and the conjunctiva are subject to hereditary influence. This was based on the following irrefutable points:

1. Atopic reagins have been found in children of atopic parents prior to the onset of the atopic symptoms in the children (Baldwin, L. B., and Brown, Aaron).

2. In two atopic individuals reagins to the same atopen may be demonstrated; for example, to that of a pollen, yet one of these individuals may suffer from hay fever alone, the other only from bronchial asthma.

3. An overdose of an atopen, injected intracutaneously or subcutaneously, may in one subject cause only symptoms of hay fever, and in another those of asthma, with or without urticaria.

Shannon[32] shows that any foreign protein may be demonstrated in breast milk. In 1923 Herrmann[33] tried to show the passage of ragweed pollen through the milk of cows that had fed on ragweed tops and the production of hay fever in individuals partaking of such milk.

According to Balyeat,[34] migrainous attacks have occurred in children as early as three to four years of age. The severity and frequency of the attacks increase as the child grows older. It has been shown to have an unmistakable familiar strain.

In 100 cases of migraine, a family history of migraine was obtained in 39 per cent. Sixty-nine per cent were females; 31 per cent were males. The average age of the females was 36.8 years; of the males, 37.9 years. The duration of the disease averaged 8.35 years. The average weight of the females was 140 pounds; of the males, 160 pounds. The average height of the females was 64.6 inches, while that of the males was 70.4 inches. The immediate families of

fifty-one females whose histories were obtained (80 per cent) approached seventy-two inches. The blood pressure averaged 129 80 in the females and 128 80 in the males. In fifty-one basal metabolic rate determination in females 40 per cent gave plus readings—an average of 9 per cent. Sixty per cent of the females gave minus readings, with an average of minus 10.8 per cent. In twenty-three basal metabolic rate determinations in males 26 per cent gave plus readings (average of 17.5 per cent), while 73 per cent gave minus readings (an average of minus 11 per cent). Twenty-seven blood cholesterol estimations gave an average of 225 mgm. Sixty-five per cent of the females had had one or more major operations. Seventy-one per cent of those operated upon had had laparotomies. Five, or 11 per cent, hysterectomy for fibroid. Eight, or 17.7 per cent, had had cholecystectomy. Five of this number had had cholelithiasis. Fourteen, or 31 per cent, had had laparotomy for chronic appendicitis. Thirteen, or 29 per cent, had had thyroidectomies. Nine, or 29 per cent, of the males had had major operations. Six, or 66 per cent, had had appendectomies. Two, or 22 per cent, had had thyroidectomies. Thus we find the study of 100 cases of migraine suggests that endocrine factors play a decided rôle. The majority of the patients resided in a goiter zone and had a distinct enlargement of the thyroid gland. The immediate families of the patients showed a high incidence of tallness and the male patients particularly were far above normal height (70.4 inches). The basal metabolism test, made frequently, was abnormal. The greatest relief obtained was when therapeutic efforts were directed toward the thyroid gland, such as thyroidectomy or feeding of thyroid substance.[35]

The underlying mechanism of allergy of the upper air passages suggests strongly to me that in arriving at the diagnosis one must bear in mind the endocrinopathy of the whole organism. To make myself clear, may I cite to you a few instances where endocrine dysfunction influences the allergic condition. The endocrine system plays a more dominating rôle in allergic cases, particularly in those of the upper air passages. The tie-up between the allergic disturbance and the detailed function of the endocrines is a conclusion which I draw from the following citations.

During the periods when opotherapy was omitted,[36] the patient suffered from otorrhagia and subconjunctival hemorrhage in addition to the other hemorrhagic disturbances. Owing to her negligence, an acute hemorrhagic attack occurred, signalized by metrorrhagia, epistaxis, hemoptysis and purpura; this was resistant to the classic coagulative treatment. However, when thyroid therapy was instituted,

hemorrhages were arrested. The origin of this hemorrhagic complex apparently was due to thyroid dysfunctioning.[37]

Then there is the case,[38] two months after striking the forehead against a door, copious watery mucous discharge came from the nose. Discharge would last about six weeks, then suddenly cease, only to reappear a few months later. Physical characteristics of patient suggested dyspituitarism, and when whole pituitary gland extract was administered prompt and permanent relief was established.

Maira reiterates that many years of experience have convinced him that epinephrine is the treatment par excellence for combating attacks of asthma. These patients tolerate large doses.

Analysis of 1,000 cases at the Evans Memorial, 585 of which were basically endocrine, the incidence of tinnitus aurium was 35.6 per cent of the endocrine cases and 32.7 per cent in the nonendocrine cases. Further study of the nonendocrine group showed an appreciable percentage of diseases in which tinnitus is a characteristic and not infrequent symptom. It is concluded that while tinnitus aurium is not a characteristic symptom of ductless glandular affections, it is met with equally often in hypofunction of the endocrine glands.[39]

I need only emphasize (1) the use of adrenalin chloride and epinephrine in the treatment of asthma, or urticaria and of angioneurotic edema, (2) the administration of suprarenal gland in Addison's disease, and in other states of asthenia, hypotension and hypothermia; (3) the clinical conceptions of the chromaffinopathies and the interrenopathies with their subdivisions of hyperfunction, hypofunction and dysfunction, and (4) the Loewi test and the Goetsch test in clinical diagnosis, to clinch the unescapable deduction.[10]

Bensaude and Hallion[11] have made a study of the mechanism of the asthmatic spasm by recording the variations of respiratory expansion of the lung as influenced by intravenous injections of adrenalin and pituitary extracts. Adrenalin alone relaxes the bronchioles, which explains the therapeutic efficiency of this drug in asthma. In larger doses, it diminishes the respiratory expansion, however. They thought the phenomenon was due to an excessive congestion produced in the lung and consequent pulmonary edema. It is probable that all doses of adrenalin actually relax the bronchial musculature. On the other hand, the hypophyseal extract is bronchoconstricting in large doses—doses much larger than would be used clinically. In small doses no appreciable bronchial spasm is produced: no restraint on the respiratory oscillations is observable; in fact, they

may be amplified. This latter effect of the pituitary extract is interpreted as the response of the lung to the lowering of the blood pressure induced in the pulmonary vessels. The decongestion of the lungs facilitates their expansion, which is diminished by the circulatory engorgement. The concurrence of these two effects, the relaxation of the bronchial musculature by adrenalin and the diminution of the pulmonary blood pressure by pituitary extract is a justifiable explanation of the beneficial effects observed in their use in asthmatic spasms.

Werneck[12] reports a male infant, aged three months, which had stridor from birth and was unable to take the breast properly on account of disturbance in respiration. A few days later the child was brought in asphyxiated, in deep cyanosis and apparently dead. With little anesthesia the right lobe of the thymus was removed. "It weighed 5 gm. and was macroscopically normal, but the microscope revealed histologic changes. The total weight of the thymus can be estimated 9 gm., which is within normal range, and there could not have been compression of the air passages or nerves." The stridor and other symptoms disappeared by the second day. There has been no further tendency to cyanosis following the fourth day of the operation and the child thrived. These facts help to explain beautifully the excessive endocrine functioning of the thymus as responsible for the respiratory disturbances, cured by partial thymectomy.

Thyroid, adrenal and anterior hypophysis injection tends to diminish vagus tonus and to increase sympatheticotonus. Thus it favors the appearance of peptone shock. On the contrary, parathyroid and posterior hypophysis injection increases vagus tonus; the phenomena of shock are delayed, and in the rabbit may be prevented. Thyroidectomy renders the rabbit vagotonic, and shock is not produced or is slight. After twenty or thirty days the animal is again capable of the reaction. It was shown that if one gives the thyroidless animals a thyroid injection, the capacity for reaction reappears, and when he is given parathyroid the resistance to shock is maintained.[13]

Drury[11] reviewed the literature on the possible relation of various endocrine glands to otosclerosis and discusses some of his own data obtained in a study of more than 100 cases. Two cases are reported, which confirm the fact that widely divergent factors can excite the appearance of otosclerosis in a predisposed person. The essential factor is probably a chemical undermining the nutritive stability of bone and cartilage. In a great percentage of cases the several endocrine glands are distinct etiologic factors through their influence on nor-

mal metabolism. In cases of otosclerosis without fixation of the footplate of the stapes or other irreversible organic changes, a response to the treatment of endocrines may improve the apparently hopeless condition. The influence of the hereditary tendency would seem to be a dominant factor in determining the pathology of otosclerosis where an endocrine or nonendocrine pathology produces disturbances of metabolism. The work here may suggest a possible solution of the highly complex problem of the etiology of a few selected cases of otosclerosis.

Sensitiveness in experimental anaphylaxis is increased by thyroid extract and by insulin; is decreased by parathyroid extract, adrenalin and extract of the posterior lobe of the hypophysis, and is uninfluenced by extracts of the sex glands, corpus luteum and the anterior lobe of the hypophysis. Clinical anaphylactic sensitiveness and idiosyncratic symptoms are increased in hyperthyroidism and exophthalmic goiter, and under insulin and thymus treatment; is decreased by adrenalin, by extracts of the parathyroids and the posterior lobe of the hypophysis, and in myxedema; and is uninfluenced by extracts of the anterior lobe of the hypophysis. Change in the function of the female sex glands may condition either increased or decreased clinical anaphylactic sensitiveness.[15]

Experiments made upon dogs[16] anastomosed following Tournade and Chabrol's method showed relations between anaphylaxis and adrenal secretion which were studied from two points of view; local anaphylactic shock by injecting from 0.1 to 0.15 cc. normal horse serum in the donor's suprarenal. If the animal had been sensitized there is adrenal discharge (four cases out of five), that may last from four to twenty minutes. Anaphylactic shock was produced in the donor by injecting horse serum intravenously. From five to eight minutes a slight adrenal discharge was observed. The donor's pressure almost always rose.

In guinea pigs, rabbits, sheep and cattle, castration is followed by an atrophy or failure in growth of the bones of the nose.[17]

Acquired Factors.—Among the acquired factors one may consider the age and sex of the individual, the endocrine functions, the occupation of the individual, infections, ingestion of foods and drugs, geographical location of the patient. The type of housing and heating influencing physical allergy is not without importance.

The cytologic structure of the upper air passages is composed in the main of ciliated epithelium. For the pseudostratified layer and

the columnar layer which line the nasal cavities and the paranasal sinuses abound in ciliated cells. The vibratory area by means of an effective beat, governed as it is of to and fro movements, propel the mucin from the tip of the nose to the posterior part of the nasopharynx. These movements are uninterrupted, harmonious, with a polarity of the epithelial cells always in a constant position. The epithelial layer is covered by a relatively thin layer of mucus which acts as a transport through the medium of the ciliary movement and thus secretions from the nasopharynx to the oropharynx, and finally toward the esophagus and the gastro-intestinal tract. This is one of the main avenues of transportation of the mucus which enmeshes numerous bacteria. Persistent chilling, bad aeration, chemical irritants, faulty metabolism greatly modifies the movement of the ciliated epithelium, recognized as highly specialized structures. The invasion of an organism results in a leucocytic exudation, or an outpouring of free secretions of pus from the nose and sinuses, commonly diagnosed as the ordinary head cold. The constant and repeated injury to the fine and delicate mucous membrane and its adjacent structures can only result at first in an inflammatory condition of the upper air passages when the normal physiologic mechanism is hampered. If the patient becomes heedless of this condition and the injury is continued for any length of time, an edematous condition takes place with eosinophilic infiltration. The first line of defense, which is the ciliated epithelium, is broken down and thus seriously interferes with the function of the mucous glands which take on a compensatory hypertrophy in a fragile goblet-shaped growth known as the mucous polyp. These are frequently located in the middle meatus of the ethmoid region, but may be seen in all the other sinuses, usually exempting the inferior turbinates.

The mucous membrane covering the middle meatus in histologic structure resembles the myxomatous type. It is usually more of a delicate tissue stroma. Once the edema settles in that region, it extends into the deeper layers of the tissues until it involves the basement membrane. The water-logging usually takes place in that narrow strip of connective tissue between the glandular layer and the basement membrane. If the subject is dominantly allergic, there arises a myriad of stimuli of abnormal strength constantly hammering on that relaxed area and, when the supporting stroma is so lacking, edema with the concomitant polyp formation is the result.

In the beginning of allergic cases we have polyp formation, and when these unabated attacks multiply in frequency and intensity, then secondary infections take place which increase the amount of

connective tissue in the polyp with dense infiltration of lymphocytes, eosinophiles and plasma cells. An inflammatory process has been grafted upon the allergic condition, and we have no finer culture media for a polypoid growth than an inflammatory state superimposed upon the allergic process. When we regard the nasal cavity as a dark, moist and warm area, it becomes an ideal location for polyps to multiply in an endless chain. Then suppuration in its final phase occurs. To recapitulate, we have (a) the edematous polyp, (b) the allergic polyp and (c) the allergic polyp with secondary inflammatory process, which is more quantitative than qualitative.

One of the most important of the acquired factors of allergy which has not been stressed up to this time is the proper heating and ventilation of the home.

One cubic foot of air at zero Fahrenheit can hold only 0.56 grains of water, whereas at 85 degrees Fahrenheit it holds approximately 13 grains, or twenty-three times as much. And when the temperature in private homes is raised from 70 degrees to 90 degrees in the winter time, the dry air fights for moisture, and this will explain why in some homes the wallpaper cracks easily, fresh-cut flowers fade in no time, floors crack, and high-grade furnishings deteriorate. As they crack, these crevasses are laden with dust and germs. On the other hand, specialists in diseases of the skin and the upper respiratory tract recognize the harmful effect of such dry indoor air in winter. Such diseases as eczema and other skin disorders are far more intense under such conditions, and the same is true of infections of the upper respiratory tract. These infections grow in numerical proportions when the season of artificial heating commences. It appears to be an engineering problem.

The air conditioning system offers the only solution to a more pleasant and tolerable condition of living. Moyer and Fitts[15] have given us some very interesting information in this connection.

Air conditioning is the application of methods of controlling the cleanliness, humidity, temperature and movement of air in buildings to make the air comfortable and healthful and to obtain incidentally indoor conditions that are conducive to efficiency and happiness.

Clean air is desirable for breathing, for the reason that the dust in the air coats the membranes of the nose, throat and lungs with a film which seriously affects their healthy functioning. Dust is objectionable also because it serves as a carrier of germs. In the manu-

facture of food products, drugs and other chemicals the dust that is produced may be dangerous to health.

Humidity in air is necessary for comfort. Owners and managers of theaters, restaurants, hotels, banks and the department stores realize the advantages of cooling the air in such buildings during the summer months; and they have found out that the proper conditioning of the air during hot weather increases not only business but also the efficiency of employees.

Moisture in the Air.—The water vapor in air, usually called moisture, is an important but quite variable constituent of the atmosphere, its amount in outside air depending on the weather.

Humidity.—The steam that is contained in air is the humidity. The weight of steam that the air in a given space can hold depends on the temperature and is independent of the pressure of the air.

Absolute Humidity.—The weight of the steam in air is usually expressed in grains per cubic foot or per pound of air and is called the absolute humidity.

Relative Humidity.—The ratio of the weight of steam in a given space to the weight which the same is capable of containing when fully saturated at the same temperature is called the relative humidity. Relative humidity is usually expressed as a percentage; for example, saturated air at 70° F. contains approximately eight grains of steam per cubic foot.

In buildings where comfort is essential, as in moving picture theaters, restaurants and some factories, for example, it is desirable to provide some means to reduce both temperature and humidity and, in addition, to absorb the heat given off by a large number of people and lights. Unless sufficient cold water is available from a natural source, such as an artesian well, to make it unnecessary to recirculate the water used in the air washer, artificial refrigeration must be used to provide the necessary cooling.

An air washer may be used for humidifying air in a heating system in very much the same way as it is used in a system for air cooling. In most systems it is impossible to provide the humidity that is required in heated rooms and buildings if the water sprayed into the air flowing through the air-washer is not heated. It is the usual practice to heat the water used for spraying and also the air that is to be humidified.

Silica gel has been used as an adsorption agent in a type of mechanical refrigerating system which has been adopted for household and refrigerated car purposes. It is a manufactured product having the same chemical formula as sand (SiO_2), is a hard hygroscopic crystalline substance. It has been found that silica gel, when placed above water in a closed vessel, will adsorb water vapor to the extent of 25 per cent of its own weight. When it becomes saturated and cannot adsorb any more water vapor it can be reactivated by heating, which drives out the water by evaporation.

For a number of years, in science and in industry, methods of dehumidification have been used that did not require a preliminary cooling of the air to the point of saturation, but until recently very little definite progress was made in the application of these methods for air conditioning services. The cheapest and simplest of these dehumidification methods that do not require preliminary cooling (precooling) of the air have been developed for the use of calcium chloride as the moisture absorbent. In the form of the so-called dowflake, calcium chloride is readily available in a convenient condition for use in air-conditioning equipment. Because of its strong affinity for water, this absorbent will remove the moisture from air without resorting to precooling.

Best Room Temperatures and Humidities.—It seems to be a quite common practice among householders to maintain a temperature of about 70° F. in the living rooms of their houses, without any regard to the amount of humidity in the air. If the humidity is somewhat increased over what is ordinarily in houses, there will be the same comfort and better health conditions if the temperature is 68 instead of 70 degrees F. In fact, Ellsworth Huntington, in his book "Civilization and Climate," states that the room temperature conducive to the best mental activity is about 63° F., with the humidity held as high as possible. Unless double windows are put on a house to prevent condensation of moisture, it is probably impossible to raise the humidity high enough to make one comfortable in the living rooms of an ordinary house at 63° F. It is generally recognized that the humidity in most houses is too low, especially when the heating is accomplished by the distribution of steam in pipes. It would probably be best to provide suitable equipment in houses to keep the humidity of the air at about 50 per cent of saturation. This percentage of humidity can be maintained satisfactorily without causing condensation on the glass of windows. By increasing the air velocity inside the house, a higher percentage of humidity can be maintained with-

out condensation on the glass. In winter it is not unusual, however, to find in houses humidities as low as 10 to 20 per cent of saturation.

Diagnosis.—In arriving at a diagnosis of allergy, one must take a very detailed history of the patient and his antecedents. In the history one must question the patient regarding the past illnesses, including physical injuries, which he may have suffered, influences of atmospheric changes, occupation, diet, etc. It is best to begin with a questioning of the function of all cranial nerves, from the olfactory to the hypoglossal nerves. This should be gone through with the greatest detail.

One will be amazed at the amount of significant material this sort of direct questioning can reveal. When applying the skin test one must bear in mind the false negative reactions and that a particular test may be very specific; on the other hand, some tests may give positive reactions and have nothing whatsoever to do with the underlying disturbance of the upper air passages. In arriving at a diagnosis, the following skin tests may be used: (a) the cutaneous test, (b) the scratch or intracutaneous skin tests, but (c) the patch test is the method of choice. When applying the intracutaneous tests a most complete and accurate history of the patient's reactions to sera should be at hand. Always be prepared to combat shock with the most powerful restoratives. In fact, it is necessary at times to have the syringe loaded and Esmark bandage on hand for counter attack. Eye and nose tests are admirable ways of determining serum allergy. Ephedrine and adrenalin chloride are two of the main offensive physiologic weapons when looking for an antidote. Therapeutic tests or trial methods may be required.

Treatment.—In treating the case one must regard the etiologic importance. Search for the cause, improvement then is easy. The next thing in importance is to find out the exciting agent and then try to eliminate it from the patient's environment or diet. Slow specific desensitization should be advised and always remember nonspecific desensitization has a limited clinical application. Do not treat the upper air passages alone but treat the patient as a whole. Proper, well-balanced foods with all vitamine requirements is one of the prerequisite factors.

Preseasonal desensitization in specific cases has some measure of success. Desensitization with autogenous vaccines may be helpful but cannot be relied upon exclusively. As I said before, desensitization to serum or horse asthma, cannot be accomplished to the point of

rendering injection of serum safe. A careful history check-up is vital for the patient as well as the physician's reputation. In acquired allergy, desensitization to serum can be done intravenously, and I for one recommend it with a great deal of fear and trepidation. We must treat the cause first, the environment second and the patient last. Allergic patients cannot amputate themselves from their environment and chiefly for this reason we must not give them too much encouragement.

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Symposium

BEFORE THE MIDWESTERN SECTION

OF THE

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.

ST. LOUIS, JANUARY 15, 1936.

VIII.

SUBJECT: ALLERGIC RHINITIS.*

A PANEL DISCUSSION BY L. W. DEAN, M.D., Chairman; J. J. BRONFENBRENNER, PH.D., DR.P.H., H. L. ALEXANDER, M.D., F. K. HANSEL, M.D., A. W. PROETZ, M.D., A. M. ALDEN, M.D., W. F. WENNER, M.D., H. M. SMIT, M.D., C. C. BUNCH, PH.D., B. J. MCMAHON, M.D., J. H. ALEXANDER, A.B., L. D. LINTON, B.S.

Dr. Dean: The purpose of a Panel Discussion is to bring out salient facts in connection with the subject under consideration.

We have here a group of people, each one an authority in a particular line of work that they are doing. The thought is to have each person discuss his subject, and the other people around the table will interrupt and inject a thought or a criticism as seems advisable. Those in the audience will have the privilege of writing on the pads any questions which they care to have answered, and the questions will be distributed by the Chairman of the Panel and will be answered at the close of the session.

Before the Panel begins there are a few remarks that I should like to make in order to emphasize the plan.

The treatment of an uncomplicated allergic rhinitis must be on an immunological basis. This should give a good result. If, however, the allergic rhinitis is complicated by chronic infection of the nasal

*The work done in the Department of Otolaryngology was made possible by the Ball Research Fund.

sinuses, deflected septum or chronic intumescent rhinitis, then you must add to the allergic procedure a correction of the nasal trouble. If a person with nasal polypi has a common cold, he has more trouble than one with a normal nose, and has more nasal blockage than if the nose is normal. Anything which controls the nasal pathology will benefit the allergic rhinitis. The greater the allergic factor, the less the benefit from nasal treatment. The less the sensitivity to allergens, the greater the benefit from the nasal treatment. The best result is secured in chronic intumescent rhinitis with no allergic factors. Up to this minute it has not been demonstrated that any kind of nasal treatment cures allergic rhinitis. Sometimes nasal treatments make the allergic condition worse. This is illustrated by the appearance of asthma after various nose and throat operations.

We must remember that all patients with intumescent membranes that sneeze are not suffering from allergic trouble. The fact that the patient is allergic does not mean that he has an allergic rhinitis.

In this Panel Discussion we will be very careful of our diagnosis, and in discussing these contributions we will attempt to outline what we are treating.

The fundamental concept of allergic rhinitis is an immunological one; consequently, we have asked Dr. Bronfenbrenner to discuss:

ALLERGY FROM THE IMMUNOLOGIST'S POINT OF VIEW.

Dr. Bronfenbrenner: Immunology is not an exact science. Even the most fundamental concepts in immunology are only hypotheses, and in many instances these hypotheses are not accepted by all workers in the field. This is particularly true with respect to present day understanding of the concept of "allergy."

I thought it might be best, having only a short time at my disposal, to limit myself to a few remarks concerning the basic paradox involving the relation between resistance and hypersensitiveness, which would probably be of more interest to you than any other phase I might cover in fifteen minutes.

When complex organic substances are introduced by mouth, let us say, the mucosa serves as a barrier and does not permit their absorption into the circulation on their way to the stomach, and they are absorbed only after having been denatured by the digestive juices. However, an accidental break in the natural barriers, due to physical or chemical trauma, or to inflammatory process, may permit the passage of these substances into circulation without such a change.

This may happen also by accidental or willful trauma of the skin, nasal or respiratory mucosa. Such an exposure of unprotected deeper tissues to foreign substances changes the metabolism of the tissue. This alteration in the metabolism of the tissue is specific.

Dr. Dean: Dr. Bronfenbrenner, may I ask a question?

It has happened in three or four cases that have come under my observation that following tonsillectomy there has been an allergic upset which has persisted as asthma for a number of years after the operation. The same thing has occurred after operations on the upper nasal sinuses. We studied a patient who never had an allergic upset. Tonsillectomy was performed eight or ten years ago, and, since then, she has suffered from asthma. In the same way we hear reports of asthma following the use of iontophoresis or ionization. What is the explanation?

Dr. Bronfenbrenner: I have seen a similar occurrence in the case of a child in whom severe hay fever developed following an operation on the eye. There may be two possible explanations of this: The individual may have been sensitive to certain substances prior to the operation, but, while the tissue covering remained intact, it protected him from parenteral exposure and he did not show any symptoms. The chances are that if this child were given the skin test he might have proven to be hypersensitive. This child never had any symptoms of hay fever, but once the integrity of the mucosa was disturbed by the operation there was created a site through which pollen was able to penetrate, causing allergic symptoms.

Another possibility is that the individual may not have been sensitive at all, but due to the operation and the removal of the protective covering, an unprotected site was created through which the antigen may penetrate and sensitization result.

Dr. Bronfenbrenner (resuming paper): The change which occurs as the result of parenteral exposure to the antigens, in the final analysis, consists in a specific alteration of the reaction of tissues, resulting in increased capacity to neutralize or eliminate the foreign matter in question when it is reintroduced into such an altered organism. Von Pirquet named this altered reactivity "allergy." In his monograph on this subject he states very definitely that this altered reactivity developed in the tissues—allergy—might be expressed either as an increased sensitivity (hypersensitiveness) or as increased tolerance (immunity) (Julius Springer, Berlin, 1910, p. 86). The specificity of this process is determined by antibodies which, if they are produced in sufficient amount, may appear in the cir-

culation and may be used for a passive transfer of this altered reactivity to normal tissues.

The fact that, under certain conditions, this alteration in the tissues helps in ridding the body of foreign material is responsible for considering the whole process as a protective mechanism. Such view, however, does not harmonize with many observed phenomena. For while it is generally true that repeated injections of toxic substances render the organism resistant to lethal doses, experiments have shown that under certain conditions reinjection of the same substances may produce severe symptoms and even death in the recipient. This is the more surprising in cases where the substances injected are not toxic on the first injection even if given in very large doses.

Since repeated injection of antigens may lead in some cases to increased tolerance and in others to increased vulnerability it has been early suggested as a working hypothesis that parenteral introduction of antigens may lead to the formation of two independent sets of antibodies having different properties. Such a hypothesis is superfluous since, as a matter of fact, whenever antigen-antibody reactions occur in the animal body, there always occurs an injury to the tissues of the host, resulting in both local and general symptoms of varying intensity.

Dr. Dean: When we desensitize patients for hay fever, do we increase or decrease the allergic status of the individual? When we give minimum doses of allergen what do we do?

Dr. Bronfenbrenner: Different investigators will give different answers to this question, as the matter has not been definitely settled so far. Some think that repeated densitizing injections render animals "immune" by increasing their antibody content; others, to the contrary, think that by injection of antigen we deplete the antibody content—hence they call this process desensitization.

In my opinion, we do not change the antibody balance at all; the procedure of desensitization causes certain changes which make it impossible for the toxic products to form rapidly when antigen-antibody reaction takes place in the organ. As a matter of fact, some experiments that have been carried out in my laboratory last year by Dr. Morris show that when we increase the antibody content of the animal we increase its susceptibility. On the other hand, we have found that desensitization does not lower the antibody content to any measurable extent, so that "desensitization" is a wrong term, because even a small portion of the blood of "desensitized" animals suffices to

confer hypersensitiveness by transfer to normal animals, so that they respond with acute shock to subsequent injection of antigen.

Dr. Alexander: Is it true that the skin test remains positive in desensitized persons?

Dr. Bronfenbrenner: Yes, the skin of the desensitized person remains reactive to antigen.

In order for the refractory state to affect the skin, much more time is necessary than is usually allowed following the systemic desensitization. However, the skin will fail to react if you "desensitize" it locally. If you give a tuberculin test and then repeat it in an area near the first injection there will be no response. Should you test systematically, however, you will elicit a response. In other words, time is necessary for the exchange to the blood stream. It was shown by Freund that uterine muscle and the skin are the last structures to receive antibodies from the circulation and also the last ones to give them up. All antibodies may disappear from the circulation long before they disappear from the skin.

Dr. Proetz: What is the nature of the time lapse—a few days or a few weeks?

Dr. Bronfenbrenner: In the distribution of antibodies—days usually, but may be longer, depending on circumstances.

(Resuming.) What I would like to emphasize is the fact that whenever antigen and antibody combine, there is always the response that is essentially hypersensitive. Perhaps I could make this clearer by a rather remote analogy. If, for instance, we should set fire to wood in a hearth, for the purpose of cooking, the fuel is consumed in the process, but we care little about that, because we have a certain utilitarian end in view. The same firewood, if it is set afire without this utilitarian end in view, will present a clear loss. This is remotely analogous to what happens in the case of the introduction of an antigen to a tissue previously exposed to the same antigen. The resulting reaction may vary in intensity and form, depending on the amount and nature (solubility) of the antigen, as well as on the site and rate at which introduction of the antigen into sensitized tissue has taken place. In the final analysis the availability of a sufficient amount of antigen for a rapid union with antibody will determine the intensity of the concomitant injury to the tissues.

In the case of a limited reaction, such as may occur as a result of an ordinary exposure to pathogenic microorganisms, the allergic reaction may arrest the process of infection, and we think of it as a

defensive or immune response quite disregarding the local injury to the host, which is the cause of the symptoms at the end of the incubation period in many infectious diseases. It is this reaction between the antibody and the infectious agent which gives vague symptoms in subclinical (or abortive) repeated exposures to endemic infections.

These are reactions during which the infection may or may not be controlled, but the symptoms are due to the injury to the host who has been rendered "allergic" (in the sense of Von Pirquet) by the prior exposure to the infectious agent. If, instead of bacterial antigen, we are dealing with egg-white, for instance, all we see as a result of the introduction into the sensitized animal is the general reaction caused by it, without any attending benefit, and we speak of that as an "anaphylactic" reaction.

It must be realized, however, that all "immune" animals may present symptoms of anaphylaxis if a suitable dose of antigen is introduced directly into circulation. For instance, when animals superimmunized to toxin were given small amounts of toxin intravascularly by Behring they were killed with symptoms of anaphylaxis. Animals immune to pneumococcus, and capable of resisting injection of many infecting doses of these organisms will succumb with symptoms of anaphylaxis to injection of soluble specific substance of pneumococcus. And similarly an animal resistant to reinfection with tubercle bacillus will die from systemic injection of even minute amounts of tuberculin. Thus immunity and anaphylaxis are merely different expressions of the same process. By utilizing what we know about the mechanism of this process we may minimize the phase of injury to the host. We know, for instance, that by injecting a lethal dose of antigen into a sensitized animal *rapidly* we produce fatal anaphylaxis, but if the same amount of the same antigen is injected in a diluted state and the injection is given slowly (over a period of three to five minutes), although the animal may show more or less definite symptoms, it will survive.

To sum up: The altered reactivity (allergy) may be purely harmful to the animal, as in the experimental anaphylaxis or in clinical hypersensitiveness, but this same allergic response consisting of accelerated and intensified reaction is clearly of benefit when the antigen considered is a living parasitic micro-organism, provided that under the particular circumstances the intensity of this response is not so great that it causes irreparable injury by itself.

Dr. Dean: Do any cells in the body escape this immunological process?

Dr. Bronfenbrenner: Yes.

Dr. Dean: What cells?

Dr. Bronfenbrenner: When the animal is sensitized, in the absence of inflammatory processes, the cornea and the anterior chamber of the eye as well as spinal fluid are free from antibodies. These are the only sites which escape sensitization under normal conditions, so far as I know.

Dr. Dean: Dr. Alexander will now discuss

SKIN TESTS IN ALLERGY.

Dr. Alexander: This title, "Skin Tests in Allergy," must be defined at the outset of this very brief period of discussion. The test that will concern us this afternoon will be the one that gives immediate wheal formation—the test used in hay fever and asthma, as distinguished from the "patch test," the "tuberculin test" and others used in the various aspects of allergy.

When allergy was first introduced into clinical medicine, about twenty years ago, it received immediate popularity because it was very dramatic. It promised to reveal the reason why it was that the bronchial nasal and gastro-intestinal mucosa should suffer symptoms, and what it was that caused these remote organs to have these symptoms. The means of this revelation was a skin test by which one applied the foreign substance suspected to a scratch on the skin. If positive, a wheal developed immediately. The fact that the skin was sensitive when symptoms were confined to the bronchi or to the gastro-intestinal tract, led to the assumption that all organs must be sensitive. Clinically, at least, this assumption is a fallacy. Man may be sensitive all over and may exhibit general hypersensitivity if a huge dose of a protein is introduced. From the common clinical standpoint he is not sensitive throughout but in spots. There are three particular tissues affected, namely, the mucosa of the gastro-intestinal and the respiratory tracts and the skin.

Allergic symptoms are usually confined to those three, although the meninges and other tissues occasionally may participate. Another interesting thing is that these three organs do not usually have symptoms at the same time. Asthma (respiratory tract) or eczema (skin) or gastro-intestinal disorders usually occur alone. Rarely do they all occur together.

Dr. Dean: Dr. Alexander, does a positive skin reaction indicate that a vasomotor rhinitis is allergic?

Dr. Alexander: No, it does not. May I come to that later?

Dr. Alexander (Resuming): Now, since hypersensitiveness is localized in certain tissues only, the skin may be sensitive or it may not at any given time. Therefore, the bronchi may be very sensitive to such things as horse dander, feathers and pollens, and the skin be free from sensitivity. If the skin is not sensitive, a skin test will be negative, no matter how other organs may be.

Question: How frequently is the skin test favorable in cases of hay fever?

Dr. Alexander: There are certain statistics about this. It so happens, for reasons I do not know, that in hay fever, when the nasal mucosa is sensitive to pollens, the skin is likewise sensitive in over 95 per cent of the cases. The skin is very reliable in hay fever.

In vasomotor rhinitis the skin test is positive in about 50 to 55 per cent. The same holds true in asthma. One thousand cases of allergy were analyzed with this in view, and it was found that about one-half of those with vasomotor rhinitis and asthma had positive reactions. The other 50 per cent showed no responsive antibody present in the skin. Any test that is only 50 per cent reliable is not very accurate; but if we could only count on the fact that in half the cases the skin test would be reliable, that would be something.

Unfortunately there are other considerations that come up in regard to the skin test, and one is that allergy has a patchy distribution wherever it occurs. When allergy occurs in the lungs, one has räles and wheezing in some places and none in others. The same irregular distribution has been found in the bowels. Spasm occurs in parts of the bowels and not in the rest. It comes here and there; it is patchy. By that same token, skin tests give patchy results. If one applies the same quantity of ragweed pollen or horse dander to the skin of the back, the leg, the arm and the abdomen, the reaction may be negative in one place and markedly positive in another. Here there is another difficulty about skin reactions. Let us suppose an individual shows a 4 plus reaction on the back, on the leg a 1 plus. How sensitive is the individual? He may give a 2 plus reaction on the back and none on the arm, the usual site of testing. This variability reduces the reliability of the test.

Dr. Proetz: Does it make any difference if given intradermally?

Dr. Alexander: No.

Dr. Lorente de No: Has a nonallergic a positive skin test?

Dr. Alexander: There will appear in the *Journal of Allergy* a series of 150 cases, presumably normal individuals, who were tested at the Johns Hopkins Clinic. These individuals were students and had no evidence of allergy. I have forgotten the exact percentage, but over twenty-five gave a positive skin test.

Dr. Dean: This question is one I should like to have an answer to. What is the probability of apparently normal persons who give positive skin reactions having been at some time temporarily sensitive to some allergen?

Dr. Alexander: Two things have been considered where one gets a positive skin test in such an individual. One is that at one time he was sensitive. Now the skin, as you know, is the site of antibodies in allergy. They are presumably made in the skin, and at one time there may have been a sensitivity that left this trace. It is also possible that these individuals are going to be sensitive some day and this may be the first manifestation of it.

Finally there is the temporary reaction. A 4 plus response may be a 1 plus at a later date. The very strong allergens, and these are particularly the pollens, do not vary much. At various times we get the same reactions. There are a few others—cottonseed, fish, glue, sometimes orris root and horse dander—whose reactions are fairly constant. The 2 plus or 1 plus are those with great variances.

Dr. Dean: Are positive skin tests to certain things of less significance than others?

Dr. Alexander: No. In skin tests we find one allergen has the same significance as another.

Dr. Lorente de No: To what extent is the skin test which is produced significant? Given a case of allergy in which positive reactions occur, since some skin reactions may not be specific, which of these reactions may be significant?

Dr. Alexander: There are certain ways to find out. One is to do the clinical test and expose the patient to the suspected allergen. If symptoms occur one would know. Again, as a rule, one may not have many 3 and 4 plus reactions and these are of more significance. Again, one may test for reagins to the allergen in question by injecting the blood serum of the patient into a normal skin and testing that site six hours later.

Dr. Dean: What do you think the practical clinical importance of carrying out passive transfers in connection with your skin tests?

Dr. Alexander: I think if there is any doubt, as there often is, a passive transfer will settle the question.

Dr. Dean: What is going to be the result of testing the citizens of Berlin for skin sensitivity to ragweed pollen?

Dr. Alexander: In ragweed pollen, theoretically you should have 100 per cent negative results. There is no ragweed outside of the United States.

Dr. Alden: Is it not true that the severity of the symptoms the patient may have exhibited is in no sense a criterion of his skin test. Do reactions not vary greatly?

Dr. Alexander: Anyone with a marked hay fever has a skin so sensitive that if you dilute the extract of pollen 10,000, 100,000 or even 1,000,000 times, you may still get reactions. Reactions of the skin to dilutions of 1 to 10,000,000 are not very uncommon. So when it comes to pollens, it is very difficult to correlate them in clinical terms with any degree of accuracy. By and large, the more reagins present in the blood, the more sensitive the patient and therefore the more severe the symptoms.

Dr. Alden: But is it not true on using a transfer test in hay fever that certain patients often manifest symptoms to pollens, yet they may have no reactions?

Dr. Alexander: When the skin is saturated with antibodies they spill into the blood and these cases are very sensitive; when not sufficient antibodies occur to induce reagins for passive transfer symptoms may still occur.

Dr. Dean: But do you ever have a patient with a 4 plus positive passive transfer of ragweed pollen with a not severe case of hay fever?

Dr. Alexander: I have never seen one; the more reagins the more sensitivity and symptoms.

Dr. Alexander (Resuming discussion): To conclude, I would say that the skin test is a very fallible, uncertain and difficult one to properly interpret.

Question: What is the apparent value of the scratch test over the intradermal test?

Dr. Alexander: I interpret this question to mean which is the more sensitive test? When it comes to its value, the scratch method is so much more simple and with pollen the scratch test is entirely adequate. The intradermal test is the more reliable, since many more reactions are obtained with it.

Dr. Dean: Many of these men present in the audience do not live in places where there are allergists or immunologists who are conversant with the subject of allergy. Is it safe for them to assume that they can make the skin test? What is your reaction to the significance of the skin test which might be made by someone who has not had the opportunity of making a careful study of the subject?

Dr. Alexander: I think anyone can test to pollens with the scratch test. The thing to be accomplished, after all, is to be able to have some practical method of testing these patients in some way without having to resort to a very awkward, difficult test. One may spend a long time to acquire experience with skin tests. That is what allergists do. They learn to know, in time, which is false and which is not, and which may be significant, and how to check, but to do that they have to spend a great deal of time and thought. On the other hand, one may just use the pollens and a few others of the hundreds of allergens. There are really comparatively few which cause trouble in the majority of individuals; bedding, pillows, orris root, animal danders and a few common foods. After all, when allergists have completed their extensive tests, what do they do? They cover the bedding; they take the pillows away; forbid access to the cat or to the dog. Under such simple requirements, most patients do very well indeed. One can do all that without skin tests, or one may take a few common things, pillows, feathers, animal danders, orris root and a few common foods and make the test with only these.

Question: In skin testing, do you advocate single or multiple syringes? Do you think it necessary to have eighty-five syringes, or do you use one? If you want to use one, can you not wash it out thoroughly and dry it, and then dilute your antigen with water?

Dr. Alexander: The test must be done properly or not at all.

Question: In skin tests for allergy, do we have false positive and false negative tests?

Dr. Alexander: In normal individuals we have positive reactions which have nothing to do with the symptoms at hand, or the bronchi can be extremely sensitive and the skin not. You may have a false positive or negative test. The reason, we do not know.

Dr. Dean: Dr. Hansel will discuss the subject

SURGICAL TREATMENT OF THE NOSE IN ALLERGY.

Dr. Hansel: In the diagnosis and treatment of the inflammatory diseases of the nose and paranasal sinuses, the high incidence of aller-

gy warrants the consideration of this factor in a great many of the cases. In 1,000 routine cases we[1] have found the incidence of allergic disease about 40 per cent among all complaints referable to the nose and paranasal sinuses. Similar studies by Baum,[2] in a group of 2,000 patients, have shown an incidence of allergy of 27.3 per cent among the nasal and sinus cases. In nonallergic patients in whom operative procedures are anticipated, it is customary, after careful preliminary studies, to proceed with the necessary interference. In allergic patients, however, it is advisable, as a rule, to institute treatment by allergic methods before resorting to operative interference of any kind. It is important, therefore, that a definite distinction be made between these two groups of cases.

It should be pointed out that, as a rule, an accurate diagnosis can be established only after a careful study of the clinical history and evaluation of the findings obtained by rhinoscopic examination, repeated cytologic studies of the secretions from the nose and paranasal sinuses, x-ray examination, with or without the use of lipiodol, histopathologic examination of pathologic tissues in the nose and the bacteriologic and biochemical examination of the nasal and paranasal sinus secretions. On the basis of these studies, the presence or absence of infection can be determined. Acute infections can be distinguished from the chronic, and infection confined to individual sinuses can be disclosed. In addition to those studies confined to the nose and paranasal sinuses, the allergic state of the patient should be known regarding the family history, the occurrence of other manifestations of allergy in the past and those in the present history associated with the nasal symptoms, the contact history and the results obtained from performing a series of skin tests. The possible part played by secondary factors which concern foci of infection, endocrine disorders, fatigue, nutritional states, etc., must also be taken into consideration.

After all these data have been accumulated and evaluated, treatment primarily concerns the management and control of the allergic state of the patient. When, after a certain period of observation, the allergic symptoms have subsided or have been brought under control to the point when they are only of mild degree, repeated observations of the nose and paranasal sinuses must be made to determine what alterations have occurred in the pathologic changes. These subsequent examinations usually show a decrease in the swelling of the turbinates, often the subsidence of edematous thickenings and small polyps in the middle meatus, and a decrease or disappearance of the edematous changes shown in the x-ray examination of the sinuses. If, in spite of the satisfactory control of the allergic symptoms, polypoid thickenings

and gross polyp formations persist in the middle meatus, they should be removed. If there is a deflection of the nasal septum which is producing obstruction it should be corrected. The persistence of marked pathologic changes and complicating infection in one or more of the paranasal sinuses may require conservative or radical operative procedures.

It should be emphasized that operative procedures upon the nose and throat, especially upon the nose and paranasal sinuses, have failed, except in isolated cases, to relieve asthma. Such operative procedures have also consistently failed to relieve the nasal manifestations of allergy. All operative procedures on the nose and paranasal sinuses, therefore, should be performed with the idea of restoring function and eliminating infection, basing the indications upon the existing symptoms and pathologic changes just as if an allergic condition did not exist. Although rather marked pathologic changes may exist in the nose and paranasal sinuses in allergy they may subside under allergic management and may not require operative procedures.

In analyzing a large group of allergic patients and reviewing the observations reported by others, it is noteworthy how many patients have been subjected to operative procedures before allergic studies or allergic methods of treatment have been instituted. Many of these patients have had necessary surgical operations, others have been subjected to surgical interference unnecessarily. In a group of 220 patients whom we have had under our observation and who were treated primarily by allergic methods, we found that the following surgical procedures were necessary. Before coming under our observation the following operations had been performed: Removal of nasal polyps, 10; submucous resection, 9; spheno-ethmoid exenteration, 4; Caldwell-Luc, 2; and intranasal antrum operation, 3. After having treated the entire group by allergic methods the following operations were performed: Removal of nasal polyps, 25; submucous resection, 10; spheno-ethmoid exenteration, 3; Caldwell-Luc operation, 3; intranasal antrum windows, 7. In this group of cases, 20 patients had their tonsils removed and 8 were subjected to tonsillectomy while under observation. On the whole, it was evident that a comparatively small number of surgical operations were necessary in this group of 220 cases.

Since each case is an individual problem, no specific rules can be formulated as to the indications for conservative or radical surgery on the nose and paranasal sinuses.

Coates[3] makes the following distinction between conservative and radical surgery. He states that conservative surgery for one pathologic condition may also be too conservative for one of different pathology, but certain types of operative procedures are easily classified as being definitely of one or the other type. All external operations are considered as of the radical type, but some types of intranasal surgery are radical as far as the element of danger and the amount of destruction of tissue are concerned. In general, conservative surgery aims to restore the individual sinus to normal function by establishing proper ventilation and drainage with the least amount of destruction possible On the other hand, radical surgery may result in the destruction of the sinus as a functioning cavity, especially the ethmoid cells, or it may entail the removal of large parts of the bony wall and all the lining mucosa.

Coates classifies as conservative those operative procedures employed for the correction of septal deflections, removal of polypoid hyperplasias and polyps, removal of portions of the middle turbinate that cause obstruction to ventilation and drainage, the opening of individual ethmoid cells by removal of small portions of the inferior or mesial walls, enlarging the ostia of the frontal or sphenoid sinuses, and window openings through the mesial wall of the maxillary sinus in the inferior meatus. He classifies radical operations as those having an external approach by means of which the entire lining mucosa of such sinuses as the frontal, ethmoid, sphenoid or maxillary sinus is removed with the object of eliminating all diseased tissue. Intranasal procedures which accomplish the same purpose are also considered as radical, for example, a complete intranasal ethmoidectomy with or without removal of the middle turbinate, removal of the entire anterior wall and floor of the sphenoid sinus, or the Halle and Canfield intranasal operation on the maxillary sinus. The Caldwell-Luc or Denker operation is the radical procedure usually employed on the maxillary antrum. External operations on the frontal sinus, including at the same time exenteration of the ethmoids and sphenoids as described by Killian,[4] Lynch,[5] Sewall,[6] Lillie and Williams,[7] are also of the radical type.

Skillern[8] divides the indications for radical surgery into the absolute and the relative. Except in those cases in which an emergency procedure is indicated, conservative measures should always be thoroughly tried before radical operation is decided upon. Coates states that absolute indications may be present in either acute or chronic cases, but in the acute types the most conservative treatment, even when surgical, is the best and safest. An absolute indication for

radical operation with either acute or chronic infections depends upon the existing evidence of serious complications, especially the intracranial types, such as brain abscess of the extra- or intradural type, meningitis or osteomyelitis. Most cases of orbital cellulitis that do not respond to conservative treatment require radical procedures. Other eye disorders, such as those which involve the optic nerve, may require radical surgery upon the posterior ethmoids and sphenoids.

It cannot be too strongly emphasized that in deciding upon conservative or radical procedures upon the nose and paranasal sinuses the diagnosis must be accurately established upon the basis of the clinical history, the x-ray and other laboratory findings, especially the bacteriologic examination and cytologic study of the nasal and sinus secretions.

In the final analysis and evaluation of the indications for surgical procedures in all sinus cases it should be remembered that the possibility of the allergic factor always exists and the question of primary importance which arises is whether the pathologic conditions in the nose and paranasal sinuses are the result of a pure allergic process, a primary infection, or a combined allergic and infectious condition.

It has already been emphasized that before the institution of any operative interference upon the nose and paranasal sinuses or the tonsils, in allergic patients, the symptoms should be controlled by allergic methods of treatment. In the event of an acute exacerbation of symptoms, anticipated operative procedures should be postponed. Allergic patients should not be subjected to operative procedures, even to tonsillectomy, during the hay fever seasons. The patient who, for example, has ragweed hay fever, should not be operated upon during the tree or grass as well as the ragweed hay fever seasons. Patients with perennial nasal symptoms but who do not have hay fever also should not be operated upon during the hay fever seasons, for instances have been reported in which hay fever and asthma developed for the first time as a result of operations performed during these seasons of the year.

As a rule, the allergic patient presents himself for treatment during an acute exacerbation of symptoms, at which time the degree of swelling of the mucosa, including the amount of edema and polyposis present, may be greatly exaggerated. At this time there is also a great deal of nasal discharge. In the evaluation of the nature of the symptoms during acute exacerbations, the question always arises as to whether the reactions are allergic or whether an acute infection

is present. On the basis of the clinical history, the appearance of the nasal mucosa and the discharge, it is frequently possible to distinguish between these two conditions only on the basis of a cytologic examination of the secretions. As already pointed out, a pure eosinophilic response indicates an allergic exacerbation. The presence of a large number of neutrophiles with only a few scattered eosinophiles indicates an acute infectious process. The presence of a large number of both types of cells indicates either the subacute stage of an infection or the retention and stagnation of the secretions during an acute allergic exacerbation with marked obstruction. In this latter instance the neutrophiles very promptly disappear with the subsidence of the obstruction and retention of secretions. In the subacute infectious process, however, the neutrophiles disappear very gradually. The eosinophiles, on the other hand, gradually increase in number. By following these principles of diagnosis, the mistake of subjecting patients to operative procedures on the basis of an assumed pansinusitis can be avoided. By the cytologic study of specimens of secretions obtained from individual sinuses, infection of a subacute or chronic nature, which may be confined only to them, may also be determined.

Assuming that the patient has been carefully studied and observed, that the symptoms have been controlled by allergic methods and that no acute or subacute infection is present, operative procedures may be instituted in those cases with positive indications.

Submucous Resection.—There is a certain percentage of patients with the nasal manifestations of allergy in whom submucous resection of the nasal septum is indicated. A deflection of the septum may play the most imporant part in producing obstruction of one or both sides of the nose or predispose the sinuses to complicating infection. It should be taken into consideration that a slight or moderate degree of deviation of the septum may, in conjunction with swelling or edema of the mucosa of the lateral wall of the nose, produce a great deal of annoying obstruction. It is important in these instances to evaluate the part played by each of these two factors. If the obstruction is relieved by the control of allergic symptoms and the subsidence of the swelling and edema of the mucosa, submucous resection of the septum is not necessary. In the event that obstruction still remains after appropriate treatment, however, this operative interference is necessary to relieve the obstruction. A deviation of the septum in those patients who have only seasonal hay fever may be a factor in producing marked obstruction during the hay fever season but may produce no symptoms at other times of the year. In some of these cases a correction of the septum may be necessary to relieve

that obstruction which becomes very pronounced during the hay fever season.

Removal of Nasal Polyps.—Approximately 25 to 30 per cent of all patients with the nasal manifestations of allergy, including those with asthma, develop nasal polyps which require removal in the majority of cases. The indications for removal are based upon the degree and extent of their formation and upon their chronicity. During acute exacerbations of symptoms or during acute infections the extent of the polyposis may be considerably exaggerated. The patient should first be treated from the allergic standpoint and should be observed over a sufficient period of time before the indications for the removal of polyps should be evaluated. Acute edematous thickenings in the middle meatus may result from an acute allergic exacerbation and are most frequently observed in hay fever patients. Acute edema, even with definite polyp formation, may also occur with acute infection in cases in which these changes had previously not been present. It is evident that these acute swellings should not be removed. If repeated observation has shown that edematous thickenings and polyps are chronic and permanent in type and persist in spite of allergic therapy, they should be removed. Marked edematous thickening and definite polyp formations, however, may disappear with the control of symptoms by allergic methods. If the polypoid formations produce obstruction and retention of secretions, secondary infection may become established in the nose and paranasal sinuses. The cytologic examination of the secretions may show a persistence of a considerable number of neutrophiles along with the eosinophiles in the secretions. In these cases the problem presents itself as to whether chronic infection is saprophytic, resulting from the stagnation process, or whether it is a suppurative process with definite pathogenic infection. In these cases the nasal polyps should be entirely removed without resorting primarily to any operative interference, with the paranasal sinuses. Not infrequently it is also necessary to remove a part of the middle turbinate, especially if cystic. Cysts, however, may be thoroughly exenterated from the turbinate, preserving the soft tissue. Following the removal of nasal polyps ventilation and drainage of the sinuses should become established within a period of three or four weeks. The postoperative inflammatory process, however, may result in the persistence of a considerable number of neutrophiles in the secretions for as long as six or eight weeks. After this period of time the sinuses should be carefully studied in order to determine the extent and nature of the changes which may persist. The secretions from individual sinuses should be examined

if the presence of infection is suspected. It may be necessary to puncture and wash the maxillary antrums, first aspirating the secretions for cytologic, biochemical and bacteriologic studies. The sinuses should also be studied from the x-ray standpoint, with or without radiopaque injection. From an analysis of these findings, operative procedures upon the paranasal sinuses should be based.

Indications for Operations Upon the Maxillary Antrum.—If there is a persistence of chronic infection, markedly thickened mucosa and polyps in the maxillary antrum, operative interference is necessary. Infection in the maxillary antrum as a result of its extension from the root of an infected tooth should always be taken into consideration. The choice between intranasal conservative procedures and radical interference depends upon the degree and extent of the pathologic conditions.

The intranasal procedure in which a window is resected into the inferior meatus may be necessary in those patients who are subject to repeated acute infections during which the symptoms relating to the maxillary sinus are especially pronounced. In chronic cases the intranasal procedure establishes ventilation and drainage and usually produces satisfactory results. In the event that satisfactory results have not been obtained, the radical type of operation is more simplified, because the intranasal procedure will have already been performed. There is a great deal of difference of opinion as to the indications for conservative and radical operations. The value of the conservative type of operation upon the maxillary sinus has been emphasized by Tucker,[9] Lewis,[10] Carter,[11] Hempstead,[12] and many others. More recently Goodyear[13] reported his experiences extending over a period of six years, on a group of eighty-four cases in which the intranasal antrum operation was performed. Goodyear had formerly employed the Caldwell-Luc operation as the one of choice. In comparing the two types of procedures he states that although the Caldwell-Luc operation is indicated in certain cases, the intranasal procedure has convinced him that in many instances the end results are equal and even superior to those obtained by the more radical operation. He noted that even in cases in which a very marked thickening of the antrum mucosa existed at the time of the intranasal procedure this pathologic process entirely cleared up. Although recent experimental and clinical observations have shown that there is a regeneration of the antrum mucosa following its removal by radical operation, not infrequently the regenerated mucosa consists of thickened fibrous tissue and functionally does not approach the normal. According to the experiences of Kern and Schenck,[14] this regenerated

mucosa may become not only markedly thickened but may also become infected.

Indications for Operative Procedures Upon the Anterior and Posterior Ethmoid and Sphenoid Sinuses.—In previous papers the clinical and histopathologic phases of hyperplastic or polypoid changes in the ethmoid and sphenoid sinuses have been discussed in their relation to allergy.[15, 16] Skillern,[17, 18, 19] Sluder[20] and others have classified the inflammatory diseases of the ethmoids into three types, namely, (1) the suppurative, (2) the hyperplastic, and (3) the combined hyperplastic-suppurative. It is noteworthy, however, that the allergic factor was not considered. In a recent comprehensive discussion of the problem of the ethmoid, Coates[21] has emphasized the important part that allergic disease plays in these conditions, not only from the standpoint of diagnosis but from the standpoint of treatment.

In allergy the changes in the ethmoid cells are characterized by the occurrence of edema and rarefaction of the cellular walls, complicated or uncomplicated by infection. In cases of nasal polyps, it has already been pointed out that the principal involvement is in the mucosa of the middle meatus and the anterior ethmoid cells. In the treatment of nasal polyps an attempt is made to remove them completely with their attachments from the middle meatus. In this way ventilation and drainage of the ethmoid cells are established and in the absence of a chronic suppurative process complete resolution usually takes place under allergic therapy. Sometimes the postoperative application of radium is indicated.

In his method of conservative treatment for the hyperplastic diseases of the ethmoid, Skillern[19] advocated the removal of the middle turbinate followed by the local application of colloidal silver preparations.

In the conservative treatment of the ethmoid in allergy, the middle turbinate should not be removed. It may be necessary, however, to remove cystic portions of the anterior end to establish ventilation and drainage of the nasofrontal duct region.

In those cases of ethmoid involvement complicated by chronic suppuration, conservative treatment may fail, hence radical exenteration of the cells must be performed. Skillern[17] has called attention to the difficulty of removing all cells completely in the intranasal radical type of operation. In the external radical type of approach, as described by Lynch, Sewall and others, the ethmoid cells may be

more completely removed in their entirety. In the radical treatment of hyperplastic conditions of the ethmoid and sphenoid, Sluder advocated the removal of the middle turbinate, the complete exenteration of both anterior and posterior ethmoid cells along with the anterior wall and part of the floor of the sphenoid. These radical types of ethmoid and sphenoid exenteration are rarely indicated in allergic cases and should be employed only in those instances of complicating suppuration. In 220 cases of nasal allergy in adults we found it necessary to perform a spheno-ethmoid exenteration in only three instances.

Indications for Operation Upon the Frontal Sinus.—Although edematous changes occur in the frontal sinuses similar to those in the antrum, ethmoids and sphenoids, operative procedures are not so frequently indicated. Perhaps the dependent type of drainage in the frontal sinus predisposes it less to complicating infection. Headache referred to the region of the frontal sinuses is a frequent symptom of the patients with marked nasal obstruction. Marked edema and polyposis in the middle meatus predispose to the retention of secretions. Not infrequently it is necessary to remove all pathologic tissue obstructing the nasal opening of the nasofrontal duct or to enlarge this passage by the intranasal type of operation, in order to establish adequate drainage and ventilation. If conservative methods fail to eliminate infection from the frontal sinus, it is necessary to perform the external radical type of operation. In our experience we have rarely found this necessary. In the x-ray examination of the frontal sinuses in those cases with marked pathologic changes in the middle meatus it may be very difficult to introduce radiopaques, but after the conservative removal of intranasal obstruction or after enlargement of the nasofrontal duct radiopaque substances may be readily introduced for diagnostic purposes.

Summary.—In the final analysis of the operative indications upon the nose and paranasal sinuses in allergy, it is evident that each and every case presents an individual problem. Primarily, allergic methods of treatment must be instituted. The pathologic conditions still remaining after appropriate treatment may require either conservative or radical procedures. In addition to a careful analysis of the clinical history, every available laboratory procedure, especially the x-ray examination correlated with cytologic, bacteriologic and, if possible, biochemical studies of the secretions, should be carried out in order to utilize valuable information which cannot be obtained from the clinical history or from the direct inspection of the nose and paranasal sinuses.

Dr. Hansel: In 1,000 routine cases in office practice, I found the incidence of allergic disease about 40 per cent among all complaints referable to the nose and paranasal sinuses.

Dr. Dean: How did you determine that, Dr. Hansel? What was your reason for saying 40 per cent were allergic?

Dr. Hansel: They were definitely proved cases.

Dr. Dean: By history?

Dr. Hansel: By history and by examination.

Dr. Dean: Is a moderate increase in eosinophiles in the nasal secretions significant of allergic rhinitis?

Dr. Hansel: The significance of a certain number of eosinophiles and their relation to neutrophiles must be determined by individual experience. On account of the irregularity of distribution their significance cannot be accurately determined in terms of percentages.

Dr. Dean: In examining apparently normal individuals who have a negative history as far as allergy is concerned, we have found often a slight increase in the eosinophiles which is not ordinarily noted in nasal discharge.

Dr. Hansel: The finding of an occasional eosinophile in normal nasal discharge is not significant. We have consistently found that the presence of many eosinophiles is good presumptive evidence of the existence of nasal allergy which can usually be corroborated by history and examination.

Dr. Dean: Do they signify that an allergic state exists at the time?

Dr. Hansel: Yes, especially in instances where there is an absence of neutrophiles. During acute colds considerable numbers of eosinophiles may be present with a very large number of neutrophiles in normal individuals, especially in children. During actue colds in patients with nasal allergy the number of eosinophiles present with the neutrophiles may not be diagnostic of allergy, except in the resolution stage when the eosinophiles begin to increase in number. In the early stage of the cold they may be entirely absent.

Dr. Dean: A patient with allergic rhinitis and sinusitis was seen by Dr. Alexander and myself, and presented some interesting features. Ten years ago Dr. Alexander advised the patient to avoid certain foods and there has been no allergic rhinitis since. Yet every time the nasal discharge is examined it shows an increase in eosinophiles. The onset occurred originally ten years ago with the measles

and the same picture was found at that time. Dr. Moore expressed the opinion that this patient presented the finest x-ray example of nasal sinusitis he had ever seen, in spite of the fact that a large number of eosinophiles were present.

Dr. Hansel: The finding of a large number of eosinophiles in the nasal secretions in diagnostic numbers in patients with nasal allergy during symptom-free periods is the rule in perennial cases. In hay fever the eosinophiles are present only during the season of active symptoms. During symptom-free periods, in the ordinary case of nasal allergy, local eosinophilia is apparently the result of very mild reactions in the mucosa which are not sufficient to produce symptoms. The same conditions apparently exist in hay fever patients who are free of symptoms during the season as a result of allergic treatment. The nasal secretions always show eosinophiles. The presence of eosinophiles in sufficient numbers to be diagnostic of nasal allergy is frequently noted in patients with other manifestations, for example, allergic headache or gastro-intestinal allergy who have no definite or significant nasal symptoms. This indicates that mild allergic reactions in the mucosa may produce local allergic changes without evident symptoms.

Dr. Dean: I hope you will pardon me, Dr Hansel, but I think it is well worth while to bring all of this out.

In patients with an acute exacerbation of nasal symptoms with an acute edematous process, how much benefit is derived from allergic treatment? How much benefit is also obtained in patients with chronic allergic rhinitis? In other words, what is the effect of allergic treatment on acute and chronic nasal allergy?

Dr. Hansel: Do you have reference to the possible changes in the pathologic condition of the mucosa?

Dr. Dean: I have particular reference to nasal obstruction.

Dr. Hansel: The development of acute edema during acute exacerbations of nasal allergy is not uncommon, especially in hay fever. With the subsidence of symptoms this acute edema disappears. Similar acute edema may occur in allergic individuals as a result of an acute upper respiratory infection. When the acute attack subsides the edema likewise has a tendency to resorb. These acute edematous swellings should be distinguished from those of the chronic type and should not be subjected to surgical removal.

Dr. Dean: Have you ever noted the disappearance of edema which had been present for many months as a result of allergic treatment?

Dr. Hansel: Chronic edematous thickening which had been present for several months, or even for more than a year, may disappear as a result of allergic therapy. Several years ago, Dr. Alexander and I had a patient with very marked edematous thickenings in the middle meatus which entirely disappeared as a result of allergic treatment.

Dr. Proetz: In those cases of polyposis which do not respond to anti-allergic measures, what are the possibilities of keeping the nose open after the polyps have been removed? Do you believe that further surgical interference should be carried out to establish breathing space? If not, what other measures should be employed?

Dr. Hansel: In those instances in which chronic edematous thickenings or polyps do not change as a result of allergic therapy, they should be removed. We have followed the policy of deferring operative procedures on the sinuses until it can be determined what improvement takes place as a result of the establishment of drainage and ventilation resulting from the removal of the polyps. Continued observations are always necessary to determine the rapidity with which polyps may recur. If the symptoms are controlled by allergic methods there may be no recurrence of the polyps. Recurrence always means that the allergic process has not been sufficiently controlled. If the allergic methods fail, radium should be used locally to increase fibrosis. This will either prevent recurrence or prolong it over a considerable period of time.

Dr. Proetz: In these cases, what are the indications for removing the ethmoid cells and opening the maxillary sinus?

Dr. Hansel: After the removal of the nasal polyps further observation with allergic therapy will determine the nature of the pathologic changes and denote the degree of improvement. The institution of conservative or radical types of surgery must depend upon the conditions actually present.

Dr. Dean: What is the effect of autogenous vaccines in cases of chronic vasomotor rhinitis?

Dr. Hansel: What response is obtained is dependent upon whether the vaccine is specific or nonspecific. Satisfactory results may be obtained from the nonspecific effect of the vaccine. It is a very difficult matter to distinguish between specific and nonspecific effects. The skin tests may be of value in determining the specificity of vaccines, especially when the immediate type of reaction is obtained.

Dr. Dean: In instances of allergic pansinusitis in which no specific allergen can be found responsible for symptoms and in which

there is a discharge of pus from the nose and sinuses, is this an indication of the existence of bacterial allergy if a reaction is obtained from an autogenous vaccine?

Dr. Hansel: The bacterial vaccines obtained from the discharge in cases of this type may give specific reactions of the immediate type in the skin test. In these instances the evidence would suggest the presence of bacterial allergy.

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Dr. Dean: The title of the next paper is

TREATMENT OF THE ACUTE ATTACK OF ALLERGIC RHINITIS.

Dr. Proetz: Inasmuch as the general treatment of allergic rhinitis is being discussed in detail by others in this group, I shall confine myself strictly to my subject, the acute attack. This phase of the disease deserves discussion not so much because it is a separate entity as because it implies an urgent call for help. The patient with an acute attack of allergic rhinitis is a miserable individual and demands relief.

These acute attacks are not confined to the vernal hay fevers but may appear in midwinter or at any other time that the individual may be exposed to excessive amounts of his allergen. The acute attacks are usually the result of a sudden over-exposure to the offending substance, such as may occur during the holidays.

It is of practical importance, therefore, to determine with all expedition what it may be. This may be a complicated procedure but often it is very simple if the patient can be seen soon enough after the onset to recollect what changes there may have been in his environment.

As the sensitivity tests may require considerable time, I resort, in the meanwhile, to a very simple chart which can be given to the patient and upon which he records his contacts—breathed and ingested—three times a day. After four or five days the record gives one a fairly accurate estimation of the patient's diet and environment and frequently supplies a short cut to relief. This careful record incidentally impresses on the patient the need of close observation. Unless special stress is laid upon them, the patient is likely to omit such articles as pepper from his list. From such a record as this, elimination diets can readily be outlined to fit the individual case. This does not take the place of the other customary tests but serves as a practical short cut.

Question: How long after contact with an offending agent may we expect vasomotor symptoms?

Dr. Proetz: I have known reactions to occur in less than twenty minutes; they may also begin as long as twelve hours after the contact. Such things as pepper and chocolate may manifest their reactions before the meal is finished.

Treatment divides itself into four main subdivisions:

First, immunization. Since this is being discussed elsewhere, I will not dwell upon it further than to say that minimal doses of the immunizing agent are ordinarily given close together. As a general thing, it is not highly successful. If inhalants are the cause, isolation from them in dustproof rooms gives quick relief. Living on the top floors of buildings or moving out of the neighborhood, however, is rarely effective as the pollens are blown far and wide.

In the second category are such vasoconstrictors as ephedrin and epinephrin, the former, if effective, being the one of choice. Too much stress cannot be laid upon the method of employing these drugs. Merely opening a tunnel along the floor of the nose with a spray is not enough. This method does not reach the vault of the nose and the relief is of short duration. As a result the frantic patient overdoes it and uses more of the drug than is necessary, at the same time irritating the membrane into further reaction. The various jellies are inefficient for the same reason.

The logical method is to put the head in the exaggerated supine position, introduce a few drops of ephedrin into each nostril and let it find its way by gravity into the vault as the nose gradually opens.

During the acute stages, three-eighths grain of ephedrin by mouth may materially reduce the amount required locally and the irritation of administering it may be avoided.

In the third category may be mentioned physical agents such as cold air and activity. Some patients obtain relief through the night by taking a walk in the cold air before retiring. Duke of Kansas City presented a patient at the annual meeting of the American Medical Association two or three years ago, whose upper respiratory channels could be controlled at will by immersing the patient's hand in buckets of hot and cold water alternately. Brisk exercise for a few minutes may open a nose which has refused to yield to other measures.

In the fourth class are what one might term local traumatic agents. This includes the well known caustics and escharotics. In earlier days silver nitrate, trichloracetic acid or chromic acid beads were used. In England, the injection of alcohol into the turbinates has recently found favor. This was introduced a generation ago by

Stein of Chicago. The actual cautery may be used or a submucous diathermic cautery by means of an insulated electrode, which leaves a thread of scar tissue in the submucosa of the turbinate.

It has been noted that following any nasal operation, or indeed more removed operations, there has been a remission of the symptoms. This may occur also in cases of fracture away from the nose. Whether this is due to an upset in the chemistry of the tissue juices due to the injury or whether it is purely a sympathetic nervous phenomenon, I do not know.

With this in mind, I have set about to produce a minimal trauma in such a manner as to affect the epithelium as little as possible. With a right-angled ossiculectomy knife I made a series of punctures in the inferior turbinate and the opposite portions of the septum, carrying them to the periosteum or the perichondrium. This was followed by a momentary free bleeding and then by a pronounced tightening up of the membrane, freeing the breathing space and allaying the irritation for a period of three weeks or more. When the puncture was unilateral, only the punctured side was affected. Dr. Smit has, I think, confirmed this observation.

Dr. Smit: Two patients were treated in this manner. In one case of ragweed sensitivity there was relief for three weeks. In the other perennial case it was two weeks.

Dr. Proetz: I have no experience with the perennial types. My patients were in the midst of acute attacks.

While this maneuver often gives immediate relief, I am not sure that it should be advocated as a treatment, in view of what Dr. Bronfenbrenner has said in regard to the possibility of producing new sensitivities by permitting new pollens to act upon a wounded membrane.

Question: How about nitro-hydrochloric acid therapy?

Dr. Proetz: I have not used it myself. There does not seem to be any very adequate explanation for such a treatment, and I do not believe it has been very successful. I think Dr. Eyermann has had some experience with it and possibly he can answer the question better than I can.

Dr. Eyermann: Dr. Beckmann first suggested this treatment for hay fever. I tried it in the subsequent year in a series of thirty-five cases with no benefit in any one. Three patients thought they felt better. From a clinical standpoint there is no evidence that the treatment is of any benefit.

The series reported subsequently by Beckmann was from observations made by numerous people throughout the country. It is noteworthy that those observers who had the fewest number of cases reported the highest percentage of good results.

Dr. Dean: Dr. Alden will discuss the question of the use of

IONTOPHORESIS IN ALLERGIC RHINITIS.

Dr. Alden: When we consider that the cells of the nasal mucosa constitute one of the most important groups of shock tissues in the body, and in addition, that they act as a reception committee to all inhaled atopens, it is not surprising that the treatment of the clinical syndrome arising from their reaction to allergic stimulation has been one of the most difficult and unsatisfactory problems of rhinology.

The term "Allergic Rhinitis" is relatively a newcomer into the field of rhinologic nomenclature. Ever since rhinologic literature began to accumulate there has been confusion in the names used to describe this and similar or almost similar nasal conditions. The terms, periodic rhinitis, rose cold, atopic coryza, vasomotor rhinitis and hyperesthetic rhinitis have all been used almost interchangeably. During the last decade, however, due to the vast amount of new information that has accumulated regarding the various phases of allergic disease and with our improved methods of diagnosis, it is now a fairly simple matter to accurately differentiate between nasal pathology that is allergic in origin and other conditions that arise secondary to infection or mechanical abnormalities. The term "Allergic Rhinitis" can be used then to describe only those deviations from normal nasal physiology that are definitely proven to be due to hypersensitivity.

These changes in the nasal mucosa are both functional and structural and are the direct result of the reaction between the sensitized cell group and the specific atopen. This reaction is, as we all know, a typical antibody-antigen response with the liberation of some histamine-like substance with all of its accompanying train of tissue phenomena. This includes, of course, the smooth muscle spasm, the local dilatation of blood vessels with its accompanying edema and exudation, all occurring in varying degrees. All of this is largely a functional disturbance and is frequently seen early in childhood, but when this allergic child has reached maturity his nasal mucosa represents merely the summation of the tissue responses to innumerable allergic insults, and this is shown as certain definite structural changes. In other words, it is illogical to expect that a biopsy taken from the

nose of an adult that had been allergic from birth would show a normal tissue picture, even during a remission of local symptoms.

With all of this in mind, a scrutiny of the various methods of treatment that have been employed in this disease shows that most of them have been used to treat only the symptoms and not the cause of the condition. Desensitization is the sole therapy that has been directed at the underlying factor, and this has been only partly successful because of the fact that about half of perennial nasal allergics show no positive skin tests.

Given, then, a case of perennial allergic rhinitis in an adult, what can we hope to accomplish toward a relief of symptoms and how can it best be done? We know that this allergic individual is allergic because of an inherited predilection for certain of his tissues to become sensitized to some thing or things and, once sensitized, to have the ability to generate a specific tissue response to contact with or stimulation by these particular things. Nothing in the form of local treatment will probably change the fundamental physiologic characteristics of this patient that go to make him allergic. Can we, then, do something locally that will make his nasal mucosa less reactive to this specific atopen or can we produce some change in his mucosa that will tend toward lessening the severity of this response when it does occur? The answer to both of these questions is "Yes."

It has been definitely demonstrated that ionization greatly lessens the sensitivity of the nasal cells to stimulation by their atopen and that resensitization of these cells probably occurs in direct ratio to the number of specific reagins present in the blood serum of the patient. Many of these patients, however, have no positive skin tests and therefore no demonstrable reagins. It would seem that ionization would at least be worth a trial in such a case. No other method of treatment of which I am aware offers any hope of relief.

What, then, of the patient who has reached adult life, but only in spite of thousands of attacks of sneezing, leaky rhinorrhea and respiratory obstruction that sometimes makes life a burden instead of a joy? A glance at the section of his nasal mucosa shows what looks like almost irreparable damage. His epithelium has lost much of its cilia, the superficial cells have undergone metaplasia largely in the direction of their replacement with cells of lower cuboidal architecture or those of the squamous type. The glandular elements of his submucosa are all herperplastic and always alert to empty their contents on the slightest specific stimulation. The walls of the blood vessels have lost their elasticity and the bulk of the soft tissue in the nose

has so increased that comfortable nasal respiration is impossible, even during periods of remission of allergic activity.

Will ionization help this patient? It has in hundreds of similar cases. The deposition of a little fibrous tissue in this submucosa which follows ionization is just enough to squeeze out the cystic contents of these glands, to give the needed support to the flabby walls of the vascular apparatus with the resultant increase in respiratory comfort and space that makes the patient say "Why was it that someone didn't think of this a long time ago?" Few of these cases require more than one or two treatments.

The figure for relief in cases of perennial rhinitis of allergic origin following ionization has varied from 60 to 80 per cent, depending upon the thoroughness of the treatment and the method of classification. The end results from the clinical standpoint have been more satisfactory than with any other form of treatment that I have had the opportunity to observe. In recommending it to the patient the clinician has to balance in his own mind the prospects for symptomatic relief as compared with the prospects for any permanent tissue damage which may accrue as the result of the procedure. In our own mind the satisfaction expressed by a relatively large number of patients leaves little doubt as to its value.

The relief obtained by ionization in the nasal manifestations of hay fever has been less satisfactory and certainly less permanent. If our conception of the mechanism of relief and resensitization of the nasal cells is correct, then the best that we can hope for in those hay fever patients whose reagin count is high is a temporary respite. However, many hay fever patients show by the transfer test, few reagins and a fair proportion of them none at all. Such patients would be much better subjects from the standpoint of permanency of results. Certainly we can say that no hay fever patient can be given any statement as to the prospect of relief following ionization except after a complete and careful allergic work-up. Upon such a basis I hope that in time we may have some means of classifying patients and giving each the form of therapy that promises the best in the way of results. Perhaps some combination of ionization and desensitization will be the answer.

There are several questions relative to this procedure that as yet remain unanswered. Why is it that ionization of one side of the nose alone often produces relief of symptoms on the untreated side? Why is it that x-rays, taken of the sinuses of an allergic patient both before and after ionization, have shown great reduction in the swell-

ing of the sinus mucosa following the treatment? What part does the sympathetic nervous system play in the response following ionization? Answer these questions and perhaps some of our problems relative to the nose will be nearer solution. These are only a few of the factors concerning ionization about which we can as yet only speculate. We have still a long way to go, but we are at least started in the right direction, and though we may fail in the end to add anything substantial to the understanding of allergy, we shall at least be all the wiser for having tried.

Dr. Dean: Do you feel if you have a chronic rhinitis with gastro-intestinal allergy, or trichinosis with an increase of eosinophiles in the nasal discharge, that that is allergy? In other words, are we not at times inclined to say that because a patient has a known allergy that a chronic, inflammatory rhinitis is allergic? A patient can have a positive Wassermann and not necessarily have the lesion in the nose syphilitic. Are you then safe in assuming that because we have a nasal condition, characterized by vasomotor disturbance and we know the patient is allergic, that you have an allergic rhinitis?

Dr. Alden: I don't think we are. However, that question has been brought up before today. The difficulty is making a definite diagnosis. The best we can do is to make a presumptive diagnosis. Given a patient who comes in and complains of recurrent sneezing, with the resultant nasal obstruction, and we do find that in the mucus of this nose a relatively large number of eosinophiles are present; then the best that we can say is that this is probably a rhinitis of allergic origin.

DR. DEAN: Dr. Wenner will present

STUDIES ON ZINC IONTOPHORESIS.

Dr. Wenner: One hundred seventy-five years ago Benjamin Franklin thought of electricity as being made up of minute particles which moved between the interstices of the molecules of the conductor. This theory 100 years ago became a fact incorporated in the law of electrolysis of Faraday, who discovered that each chemical valency of the molecule of a salt in solution carried an electric charge when the molecule was decomposed by an electric current. To these carriers of electric charges Faraday applied the word "ion." The breaking up of the salt molecule into its component ions was formerly called dissociation. This process is now termed ionization because it is more in keeping with the modern electrical theory of atomic structure.

Arrhenius demonstrated that electricity passed through a solution of an electrolyte (acids, bases, salts) breaks up the molecule into ions carrying negative charges—anions—which move to the positive pole—anode—and ions, carrying positive charges—cations—which move to the negative pole, cathode. The movement of these ions in both directions is equivalent and constitutes the electric current. Without this migration of ions no continuous electric current, whether in the electrolytic solution or in the living organism, is possible.

Electrolytes and proteins in living cells are decomposed by an electric current; $H+$, $Na+$, NH_3+, $Ca++$, etc., move to the cathode and $OH-$, $Cl-$, SO_4, etc., move to the anode. With the proteins a phenomenon known as cataphoresis takes place; they move toward the anode or cathode according to their electric charge. The proteins are amphoteric electrolytes dissociating with the formation of $H+$ and $OH-$ ions. Upon the amount of current—milliamperage—and the concentration of the electrolytes depends the degree of electrolysis. The duration and intensity of the current decides the degree of damage done the cells.

Koeppen (1933) studied the effect of small electric currents on laboratory animals. With current intensity of 24 milliamperes and potentials of 20 to 70 volts for periods of one to thirty seconds repeated up to ten times there occurred complete paralysis of the vasomotor nerve endings, ulceration of the skin in the region of the electrodes, hyalinized thrombi of the smaller vessels and capillaries of the kidney, lung and brain.

The physiologic effect of the galvanic current is due to electrolysis. In the isolated nerve the region near the anode shows a decreased excitability, while the area near the cathode shows an increased excitability. Carbon dioxide is liberated at the anode and ammonia at the cathode. With currents of 0.03 to 0.1 milliampere, 0.14 to 5.9 mgm. of ammonia per 100 gm. of nerve was formed at the cathode in one hour (Prawdicz-Neminski, 1933). The ions lose their electric charges on arriving at the electrodes and combine chemically with water to form bases at the negative pole and acids at the positive pole, thus altering the physical state of the cell protoplasm. The tissue cells at distances removed from the electrodes are not so greatly affected because the ions lost are regained from the circulating fluid and neighboring cells.

The process of passing foreign positive and negative ions through the skin and mucous membranes by means of a direct electric current is known as iontophoresis. Inchley (1921) showed that the iron con-

tent of the skin and subcutaneous tissue of the rabbit was greatly increased when a solution of ferrous sulphate, applied at the positive pole and a current of 30 milliamperes, were used. The increase in iron was determined by chemical analysis and histologically by means of the Prussian blue reaction. With solutions of cyanides, salicylates and ferricyanides placed at the negative pole the electric current caused there negative ions to penetrate the skin.

The ions of the heavy metals, as lead, mercury and zinc, being slowly moving ions, have caused controversy concerning their ability to penetrate tissue. Turrell (1922) stated that the zinc ion, immediately upon arriving at the surface of the skin or mucous membrane, gave up its charge to a faster moving ion. Experimenting with mercuric nitrate, Pack et al. (1924) obtained local lesions but no signs of penetration or absorption, such as nephritis and stomatitis. Lierle and Sage (1932) were unable to detect the presence of zinc in tissue immediately after the tissue was subjected to zinc iontophoresis. Both qualitative chemical and spectroscopic analyses failed to reveal any evidence of the penetration of zinc. Microchemical analysis of mucous membrane immediately after zinc iontophoresis, carried out by Miss Buhrmester in this laboratory, showed no trace of zinc. The histological method of Mendel and Bradley (1905) for detecting zinc in tissue was tried on mucous membranes before and after zinc iontophoresis without success. (The method of Mendel and Bradley consists briefly in forming the insoluble zinc nitroprusside in the fixed tissue.) In view of these negative results it was deemed advisable to attempt to affect a chemical combination in the tissue of the zinc and nitroprusside by means of the electric current.

To the rabbit's external ear, which was shaved the day before, was secured a short piece of glass tubing into which was placed 2 per cent zinc sulphate and the positive zinc electrode. The under surface of the same ear was placed in a Petri dish containing 10 per cent solution of sodium nitroprusside and potassium sulphide. Into this solution the negative electrode was placed. A current of 5 ma. was then passed through this system for twenty minutes. At the end of this time the treated ear was fixed in formalin, embedded in paraffin, sectioned and mounted unstained. A few sections were stained with hematoxylin and eosin. In control experiments sodium chloride solution and a platinum electrode were substituted for zinc sulphate solution and the zinc electrode.

Microscopic examination showed the presence of many brownish red granules in the skin below the epithelium and also in the cartilage of the zinc treated ears. In the control ears a few granules appeared

Fig. 1. Fig. 2. Fig. 3.

Fig. 1. Unstained section of rabbit's ear showing granules of insoluble zinc nitroprusside.

Fig. 2. Stained section from same region showing no evidence of cell damage.

Fig. 3. Section through ulcer of leg of guinea pig.

in the cartilage only. The sections stained with hematoxylin and eosin showed no evidence of cell damage.

Although the appearance of the granules of the insoluble zinc salt in the skin and cartilage is presumptive evidence of the penetration of zinc through the superficial epithelium, it does not indicate that a large amount of zinc passed through the tissues. Neither does it indicate that the zinc ion traveled great distances. The combined effect of electrolysis and zinc iontophoresis, no doubt, resulted in changes in the cells, though not immediately detectable histologically, which favored the penetration of the zinc ions. Both zinc and nitroprusside ions are slowly moving ions which soon give up their electric charges to faster moving ions, rendering them free to combine chemically with each other.

The experimental and clinical observations on the changes in the blood vessels, induced by electrolysis and the blanching of the mucosa following zinc iontophoresis, led us to make direct observations on the effect of zinc iontophoresis on the peripheral circulation in the web of frogs' feet and in rabbits' ears.

The hind foot of a frog was stretched out on a plate of bakelite which was then placed in a petri dish and covered with a 2 per cent solution of zinc sulphate. The positive zinc electrode was placed in this solution. The negative electrode was connected with cotton soaked with a solution of sodium chloride and placed around the frog's body. A current of 1.5 ma. was used. The circulation in the web of the foot was observed under the microscope.

The circulation of the blood in the web of the feet of all of the four frogs so treated definitely slowed in eight to fifteen minutes. Clumping of the red blood cells took place in forty-five minutes. The circulation was completely stopped in one hour. The circulation of blood in the web of the feet of frogs subjected to the electric current alone was not stopped. Clumping of the blood cells did not take place.

Similar experiments were carried out on the external ears of four rabbits. Glass tubes one inch in diameter were secured to the rabbit's ear. Into the glass container was placed a 2 per cent solution of zinc sulphate and the positive zinc electrode in the case of the experimental animals, and sodium chloride solution and a platinum electrode in the case of the controls. The negative electrode was placed on the abdomen. Observations were made under the low power of the microscope.

Using currents of 0.8 and 1 ma., zinc iontophoresis stopped the circulation of the blood in the capillaries of the treated areas within forty minutes. The circulation in the controls was not affected by currents of this intensity.

The circulatory disturbances induced by zinc iontophoresis probably in part accounts for the ulceration of the skin and gangrene of the feet of guinea pigs which resulted in the following experiment: The hind feet of guinea pigs were placed in a 2 per cent solution of zinc sulphate into which was placed the positive zinc electrode. The fore feet were placed in a 1 per cent solution of sodium chloride into which was placed the negative electrode. In the control experiments the fore and hind feet were placed in sodium chloride solution and a platinum positive electrode used. Currents of varying intensities were employed. The results are recorded in Table 1.

TABLE I.

Guinea Pig No.	Electrode	Solutions Used	Duration Min.	Strength of Current	Results
1	Zinc	Hind feet placed in 2% zinc sulp'te	20	2 ma.	No noticeable effect.
2	Zinc	2% zinc sulphate	20	3 ma.	Hind feet temporarily paralyzed. Ulceration of skin 3 days after iontophoresis.
3	Zinc	2% zinc sulphate	20	5 ma.	Temporary paralysis of hind legs. Ulceration of skin above treated area.
4	Zinc	2% zinc sulphate	20	5 ma.	Same as Animal 3.
5	Zinc	2% zinc sulphate	20	7 ma.	Loss of sensation both hind and front feet. Front feet edematous. Gangrene of hind feet and ulceration of skin of hind leg.
6	Zinc	2% zinc sulphate	20	7 ma.	Same as Animal 5.
7	Plati'm	1% sodium chloride	20	3 ma.	No noticeable effect.
8	Plati'm	1% sodium chloride	20	7 ma.	Temporary loss of sensation both front and hind feet. No other change.
1	1 sq. cm.	2% $ZnSO_4$	20	5 ma.	Area blanched surrounded by hyperemia—became necrotic.
2	1 sq. cm.	2% $ZnSO_4$	20	3 ma.	Area blanched. Ulceration.

The extent of tissue damage—due to zinc iontophoresis—is dependent not only upon the dilution of the electrolyte and the

strength of the current but also upon the size of the electrode. The smaller the electrode the greater the concentration of the lines of electric flux, the greater the concentration of ions penetrating the tissue. A zinc electrode of one square centimeter produces a much more pronounced reaction in the tissues than an electrode of six square centimeters. See Table 2.

TABLE II.

Rabbit No.	Size of Electrode	Solutions Used	Duration Min.	Strength of Current	Results
3	3 sq. cm.	2% Zn SO_4	20	3 ma.	Blanching followed by swelling and hyperemia. No ulcer formation.
4	6 sq. cm.	2% Zn SO_4	20	3 ma.	Slight blanching. No swelling or ulceration.
5	1 sq. cm.	1% Na Cl	20	5 ma.	Blanching followed by swelling and hyperemia. No ulceration.
6	3 sq. cm.	1% Na Cl	20	5 ma.	Slight blanching.

SUMMARY AND CONCLUSIONS.

Zinc ions, although slowly moving, penetrate the skin, as demonstrated by the method described.

Zinc iontophoresis causes disturbances in the circulation of the blood through the smaller vessels and capillaries of the skin.

The destructive changes in the skin following zinc iontophoresis depend upon the strength and the duration of the current, the area of tissue treated and the concentration of the electrolyte. In the experiments reported here the concentration of the zinc sulphate solution was not varied.

Dr. Dean: Is there any reason for thinking that the parasympathetic ganglia or nerves are involved?

Dr. Wenner: It has been demonstrated that electric stimulation produces a temporary or permanent paralysis of the vasomotor system with the degeneration of ganglion cells depending upon the duration and strength of the current. In a recent work, done in collaboration with Mrs. Alexander, the membranes of cats, one to three weeks after zinc iontophoresis, were found to fail to respond to the parasympathetic drug, acetyl beta methyl choline.

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Dr. Dean: The next paper will be presented by Dr. Smit. The title is

TISSUE CHANGES IN IONTOPHORESIS.

Dr. Smit: Iontophoresis, since its introduction more than forty years ago, drew attention to its value as a therapeutic measure only in so far as the local symptomatology was affected. Until recently little or no attention was called to the changes the process might provoke in the treated tissue. Hollender, in his clinical investigation on the effect of zinc ionization in vasomotor rhinitis, reported an initial destruction of the epithelium following ionization with subsequent regeneration of the surface epithelium, first as a squamous cell formation and within three months as a pseudo-stratified type with cilia persistently absent; the subepithelial stroma showed a gradual tendency to become more dense in structure with an early marked lymphocytic reaction, subsiding slowly, but persisting to some degree even a number of years after treatment. Hollender stated that the mucous glands showed changes in only one section. McMahon, in his experimental work on the mucosa of the frontal sinuses and nose of dogs following ionization, stated that immediately after ionization there was produced fragmentation of individual and large blocks of cells with round cells infiltrating through to the surface from subepithelial tissue; there was also a separation of tissue from the periosteum in various places. He showed that within seven weeks the epithelium returned to normal, and in his conclusion states that fibrosis of subepithelial tissue occurred which was seen to be progressively more marked in animals killed at intervals of from eighteen hours to seven weeks following ionization.

In the experimental work reported here definite changes in the nasal mucosa of dogs and guinea pigs were found to occur following iontophoresis. Attempts were made to correlate these findings with

changes that might occur in the human mucosa removed at biopsy before and after treatment. This, however, was difficult because of the pathology existing prior to iontophoresis.

Procedure.—Dogs and guinea pigs were prepared by intraperitoneal injection of sodium amytol solution. One side of the nose of dogs was packed with two long strips of cotton saturated with the electrolyte. Between these cotton strips the electrode was inserted. After preliminary tracheotomy one side of the nose of guinea pigs was filled with 10 per cent tragacanth gel to which was added 2 per cent zinc sulphate. A fine zinc wire covered with cotton was then inserted. The negative electrodes, covered with pads of cotton saturated with sodium chloride solution, were placed on the abdomen.

The current was supplied by a "B" battery, which was connected with a milliammeter and a voltmeter. The Warwick apparatus was used on some of the dogs. The amount of current used was four milliamperes for twenty minutes for guinea pigs and one milliampere minute per pound body weight for dogs.

The human biopsies were obtained from two patients who had been ionized by the Warwick method and one patient ionized using 10 per cent tragacanth gel to which was added 2 per cent zinc sulphate.

Gross Observations.—Gross changes were best studied in the human. Immediately after ionization the mucosa had a grayish appearance. Within twenty-four hours after ionization the treated side of the nose was filled with a thick mucoid appearing membrane which could not be removed without tearing the underlying tissue. Three or four days later this membrane could be removed without producing bleeding or any macroscopic injury to the nasal mucosa. Following removal of this membrane the nasal mucosa had a red, raw, beefy appearance and the turbinal tissue was usually retracted. The nasal mucosa, several days after removal of the membrane, appeared to be fairly normal in color, and in those patients in whom favorable clinical results had been obtained the mucosa was very dry.

Microscopic sections of the membrane immediately after its formation showed epithelial cells along that portion which had been attached to the nasal mucosa and the remainder consisted of a fibrinous mass. Sections of the membrane several days after its formation showed no epithelial cells.

Microscopic Observations.—1. For comparison with mucosa obtained from ionized dogs sections of normal dog mucosa were

studied. These showed normal ciliated columnar epithelium with a loose submucosal stroma in which were found numerous mucous glands, rather large venous spaces and blood vessels. (Fig. 1.)

2. The nasal mucosa of a dog which had been subjected to an intranasal cotton pack saturated with Warwick solution for nine minutes and sections obtained two hours after removal of the pack showed desquamation of the epithelium, the basal cell layer remaining intact; blood spaces were filled with a fibrinous exudate; some round cell infiltration was present in the submucosa. (Fig. 2.)

3. A dog was ionized, using the Warwick technic and four milliamperes of current for four minutes. Sections were obtained six hours after ionization. Desquamation of the epithelium had occurred. There was marked cellular infiltration with polymorphonuclear leucocytes. Marked hyperemia was present and the glandular ducts were greatly dilated and filled with a homogeneous exudate. (Fig. 3.)

4. One week after the ionization of the right side of the nose of a guinea pig with 2 per cent zinc sulphate in 10 per cent tragacanth, using a current of four milliamperes for twenty minutes, sections of turbinates and septum were obtained. (Fig. 4.) The un-ionized side of the septum was covered by ciliated columnar epithelium, beneath which was seen the loose stroma of the submucosa in which numerous glands and blood vessels were present. (Fig. 5-A.) The side that had been ionized was covered by a very compact and contracted mucosa; the epithelium was stratified squamous, the submucous was infiltrated with round cells and fibroblasts, glands were decreased in number as compared with the un-ionized side and the blood vessels were contracted. (Fig. 5-B.) These same changes were found in the mucosa covering the turbinates.

5. Six weeks following ionization in a guinea pig with 2 per cent zinc sulphate in 10 per cent tragacanth gel, using a current of four milliamperes for twenty minutes, sections of turbinate and septum were obtained. The mucosa of the turbinate on the un-ionized side of the nose was normal in all respects, whereas on the ionized side, although the epithelium was normal ciliated columnar, there was marked round cell infiltration and a very decided absence of glands. (Fig. 6-A-B.) Vertical sections of the septum were normal in so far as the mucosa was concerned; however, a perforation had occurred in the anterior third of the septum; the margins of the perforation were covered with ciliated columnar epithelium. (Fig. 7.) Posteriorly there occurred cartilaginous necrosis with repair by fibrous tissue. (Fig. 8.)

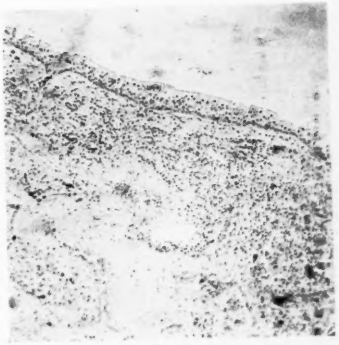
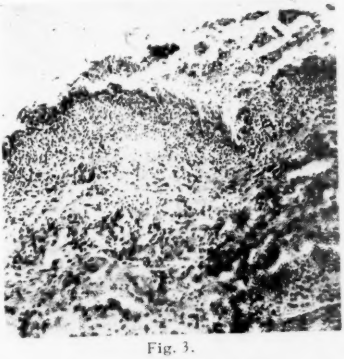


Fig. 1.

Fig. 2.



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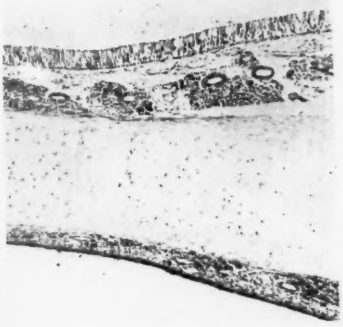

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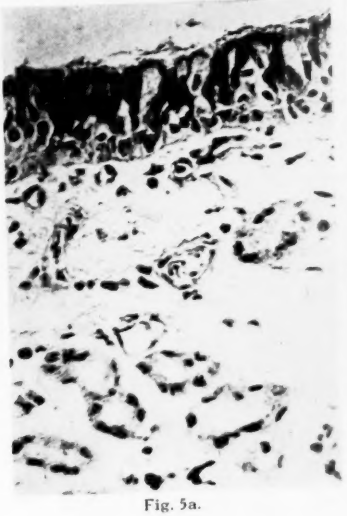

Fig. 5a.

Fig. 5b.

6. Using normal saline in 10 per cent tragacanth and a platinum electrode with a current of four milliamperes for twenty minutes in a guinea pig, sections of the septum and turbinates six weeks after ionization showed no difference between the ionized and un-ionized sides of the nose. (Fig. 9.)

7. Biopsies were obtained from the nasal mucosa just previous to and one month after ionization by 2 per cent zinc sulphate in 10 per cent tragacanth, zinc electrode and a current of six milliamperes for twenty-one minutes in a case of allergic rhinitis. Previous to ionization the nasal mucosa was very edematous, the epithelium was stratified squamous and hyperplastic; the submucosa was very edematous and infiltrated with eosinophiles. (Fig. 10-A.) One month after ionization on the same side there was a disappearance of the edema, the epithelium was a low type of stratified squamous; the submucosa was compact and there was infiltration of fibroblasts. No eosinophiles were present. (Fig. 10-B.)

8. Eight weeks after the ionization of a dog on one side of the nose by the Warwick method, using a current of seven milliamperes for eleven minutes, the un-ionized nasal mucosa appeared normal. (Fig. 11-A.) Marked changes were found on the ionized side; there was a hyperplastic stratified squamous epithelium; the submucosa was fibrotic, there was a loss of glands and many atypical glands were present, the blood vessel walls were thickened and large venous spaces collapsed by the fibrous tissue, only a small amount of round cell infiltration had occurred. (Fig. 11-B.)

9. Biopsy upon the nasal mucosa one year after ionization in a human by the Warwick method showed columnar epithelium which was ciliated in areas, the basement membrane was thickened, submucosa was fibrotic and infiltrated by round cells. There was no apparent loss of glands. (Fig. 12.)

10. This tissue was removed from the nasal mucosa of an eighteen-year-old boy one month following ionization, using the Warwick method, with a current of six milliamperes for twenty-four minutes. The patient was first seen on June 5, 1935, and presented a history of allergic manifestation, which occurred for the first time during the latter part of May, 1935. Skin tests showed sensitivity to ragweed and June grass. Microscopic sections of the mucosa showed a marked hyperplastic stratified squamous epithelium, fibrotic submucosa and metaplastic changes in the glands and their ducts. (Fig. 13.)

Fig. 6a.

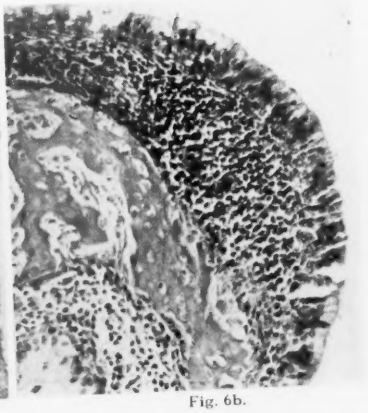

Fig. 6b.

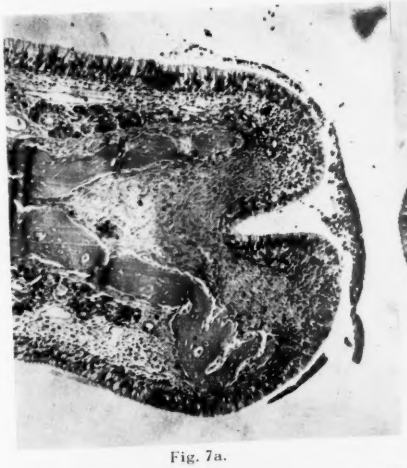

Fig. 7a.

Fig. 7b.

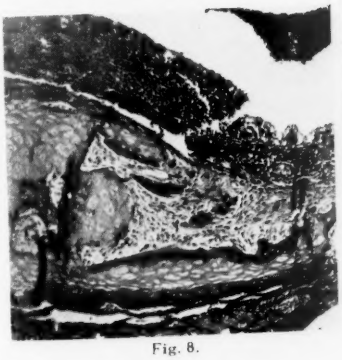

Fig. 8.

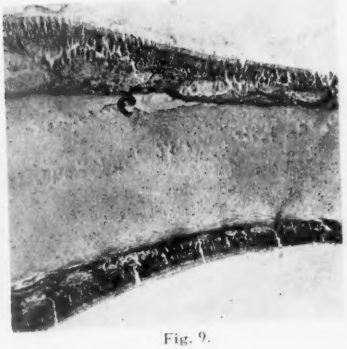

Fig. 9.

11. This is tissue from a twelve-year-old boy, one year after ionization by the Warwick method, using a current of ten milliamperes for nine minutes. This patient gave the history of his present allergic manifestations as having occurred for the first time two years previous to ionization. Skin tests showed only sensitivity to ragweed.

The epithelium was very irregular and was of the stratified squamous type. There was an attempt to form an intra-epithelial gland. The submucosa was fibrotic. Large venous spaces were present. Glandular ducts were dilated and numerous atypical glands were present. The majority of the glands appeared to be active. (Fig. 14.)

Comments.—These sections show that important tissue changes do occur following iontophoresis. The changes appear in a rather definite sequence, each being a step in the reparation of injured tissue.

Grossly one sees immediately after ionization a gray coated mucous membrane; this is probably due to the proteins of epithelial cells and exudate coagulated by the process. However, this process is more than superficial. Dr. Wenner has demonstrated conclusively that there is a penetration of zinc ions deep into the tissues. It is partially due to the actual penetration of zinc ions and also to the electrical current that coagulative necrosis in the tissues is produced. However, the mucosa does not show the same change when subjected to the same strength of current alone.

Immediately after ionization an acute inflammatory process occurs. There occurs a coagulative necrosis with sloughing of the epithelium, infiltration of polymorphonuclear leucocytes and dilatation of blood vessels. The membrane which forms is a result of this acute inflammatory process; part of it is produced by the coagulation of cells and the remainder by the exudative process. As the acute inflammatory process subsides the polymorphonuclear leucocytes are replaced by round cells. The round cells persist as long as any irritative process is present.

The denuded mucosa later becomes covered by stratified squamous epithelium in the process of reparation. Boling has shown that the stratification which occurs after injury to the nasal mucosa is produced by the invasion of dedifferentiated epithelial cells into the damaged area and that in time there is redifferentiation of these cells to reform normal columnar epithelium. This return of the epithelium to normal ciliated columnar was found to occur in guinea pigs six weeks following ionization and in one human biopsy one year after ioniza-

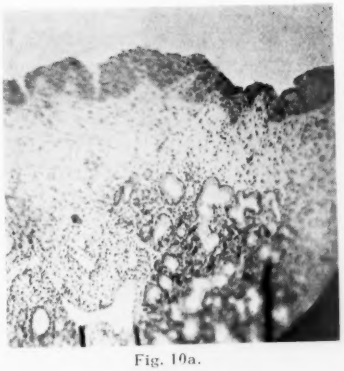

Fig. 10a.

Fig. 10b.

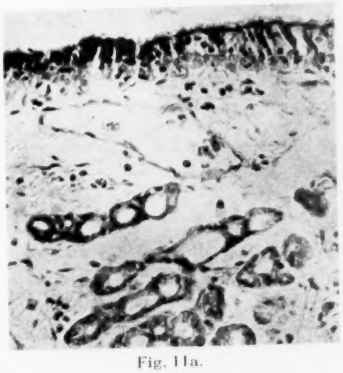

Fig. 11a.

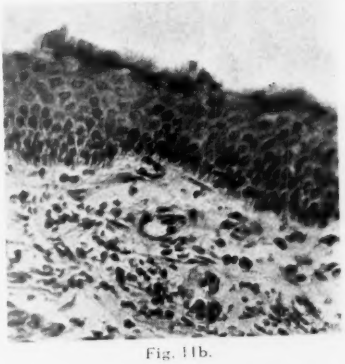

Fig. 11b.

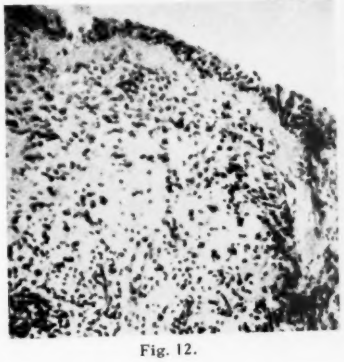

Fig. 12.

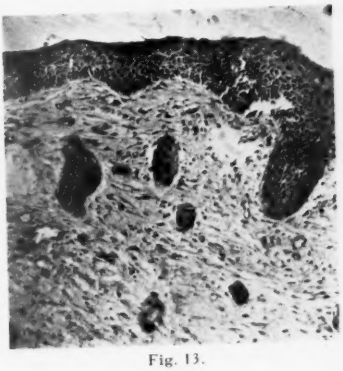

Fig. 13.

tion. Whether the epithelium returns to normal depends upon the presence or absence of an inflammatory process. If a chronic inflammatory process is present the epithelium will not return to normal. In the human there may be an existing chronic inflammatory process or one may occur as a result of ionization and therefore the epithelium may remain stratified squamous.

Approximately one week after ionization the polymorphonuclear leucocytes are replaced by round cells and there occurs infiltration of the submucosa by fibroblasts. It is also about this time that the blood vessel walls show evidence of thickening and the glands and their ducts show atrophy and metaplasia.

As the process of repair advances the fibroblasts are replaced by older fibrous tissue. It is probably the result of the contraction of this fibrous tissue that the collapse of the large venous spaces and retraction of enlarged turbinates take place. There is also some attempt to form new glands by the ingrowth of epithelium; these are atypical glands, the epithelium of which is of the nonsecretory type.

That cartilaginous necrosis can occur is shown by the perforation and necrosis produced in the septum of a guinea pig six weeks following iontophoresis. Necrosis was found also in a dog five weeks following iontophoresis; no perforation had occurred; the necrosis was on the side of ionization.

Biopsies upon the nasal mucosa of an allergic patient previous to and one month after ionization show clearly the changes occurring in an edematous allergic nasal mucosa. Dehydration of the tissues occurred following ionization. The epithelium changed from a hyperplastic stratified squamous to a low type of stratified squamous. There was an infiltration of fibroblasts and a loss of eosinophiles after this treatment. This patient clinically had a good result from iontophoresis.

Conclusion.—Summarizing the tissue changes which one finds following zinc iontophoresis there occur: coagulative necrosis of the epithelium; early stages of inflammation with polymorphonuclear leucocytes which are later replaced by round cells; atrophy of glands and loss of glands; metaplastic changes in glands and ducts; formation of stratified squamous epithelium, which later returns to normal ciliated columnar (if there is not a chronic inflammatory process present); fibrosis of submucosa; dehydration of edematous tissue; fibrosis of blood vessels and in some cases cartilaginous necrosis.

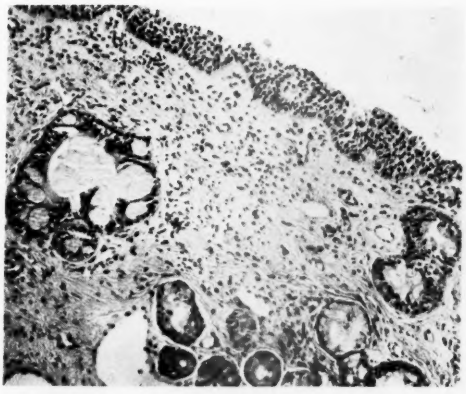

Fig. 14.

Dr. Dean: Do you think the mucous glands regenerate and become functional?

Dr. Smit: The mucous glands regenerate from the surface epithelium. These regenerated glands from surface epithelium are said to be nonsecretory, but our observations indicate that they may in time become functional.

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2. McMahon, B. J.: Late Changes in the Mucosa of the Frontal Sinuses and Nose of Dogs Following Ionization. Arch. Otolaryngology, Oct., 1935.

3. Boling: Regeneration of Nasal Mucosa. Arch. Otolaryngology, Dec., 1935.

Dr. Dean: Dr. Bunch will next discuss

THE PRINCIPLES OF THE ELECTRIC CURRENT IN IONTOPHORESIS.

Dr. Bunch: The principles governing the action of the electric current in iontophoresis are based upon a peculiar combination of fact and theory. The actual nature of the flow of an electric current is not fully understood. Why an electric current flows at all, why it will pass through a conductor and not through an insulator are theoretical problems, as is the actual nature of electricity itself. We do know that when the proper conditions have been met the current does flow and it is on an accurate knowledge of the effects of its passage through conductors that much of the electrical industry is based.

By physical definition, matter exists in three forms, solids, liquids and gases. Since the materials used for nutrition and growth reach the cells in a liquid form, let us assume that the various parts of the body have the properties of a liquid conductor. If this assumption is accepted, it is possible to account for the action of the electric current in iontophoresis on the basis of the principles set down by Arrhenius. This investigator assumed that the molecules of liquid conductors carry positive and negative charges of electricity which are in equilibrium when no chemical action is taking place. If some outside force is sufficient to overcome the balance between the positive and negative charges in the molecule, an electric current will be set up between two connected unlike electrodes placed within the solution. The parts of the molecule, called ions, which carry a positive charge, will be attracted and move toward the negative pole of the outside disturbing electrical force, and those carrying a negative charge will move to the positive pole. The speed with which these ions travel varies in different solutions, but is constant for identical conditions, and a very careful table of their speed and other characteristics has been worked out. If molecules which do not carry electrical charges be introduced into the solution, the speed of the ions may be decreased or stopped. Also if a slow moving ion should collide with one having potentialities of faster motion, the latter will take the charge from the slower moving ion and start its faster motion, the slower moving ion losing its charge and coming to rest. These principles govern the action of the electric current and the solutions in iontophoresis. (For a more accurate and detailed description of the processes in ionization, the reader is referred to any modern text in electrochemistry.)

Iontophoresis is defined by Worland as "the introduction, by means of an electric current, of ions of different sorts into the tissues of the body for therapeutic purposes." For the fulfillment of the conditions implied in this definition it is necessary that the ions shall be in intimate contact with the tissues so that their movement will not be retarded under the action of the electric current. The current must be unidirectional, i. e., it must be direct current rather than alternating. If alternating current is used, during one instant the stream of ions will flow toward the body tissues and during the next in the opposite direction, and the integrated value of its ionic action will be nil. The number of ions which will enter the tissue will be determined by the area of the surface in contact with the solution, the strength of this solution, the amount of current and the time during which the action takes place.

In iontophoresis of the nasal cavities the surface area is determined by the manner in which the electrolyte is placed in the cavities. If air pockets exist between the electrolyte and the tissue, the ions will not pass this barrier. Should the electrode itself come in contact with the tissue, the current will be largely short circuited and fail to pass through the electrolyte. The current strength should be maintained at a level where pain will be minimized and actual cautery will not take place. The solutions should be of the proper concentration. Each of these variables should be determined for the basis of scientific procedure.

The recent impetus to the use of the zinc electrode and the zinc sulphate solution in nasal therapy appears to have been taken from the procedure adopted by Friel,* who has used this method in the treatment of suppurative otitis for a number of years. I have been unable to locate in the literature experimental evidence for the addition of tin, copper, cadmium or other metals to the electrode or the electrolyte, although there may be indications for their use.

Friel advocated the use of from three to four milliamperes of current for ten minutes in treating ears, but if the patient complained of pain or discomfort, the current was reduced to two or even one milliampere and the time lengthened accordingly. I cannot locate in the literature the reason for basing the amount of iontophoresis on the weight of the patient. The technic used by some is to give a "dosage" of one milliampere per minute per pound of body weight. This technic may have a reasonable background if the results to be secured are systemic, for many drugs are prescribed according to this formula. For example, if the patient weighs 140 pounds, this procedure might call for a current of fourteen milliamperes for ten minutes. In many patients a current of fourteen milliamperes causes discomfort or pain. To obviate this, the same dosage might better be given at the rate of five milliamperes for twenty-two minutes with a minimum of discomfort. If the effects of the iontophoresis are considered to be local in character, it is unnecessary to consider the body weight but simply the area with which the solution comes into contact, the concentration of the solution, the current strength and the time.

The nature of the reaction, whether it be local or systemic, is a problem waiting solution. It seems probable that it is both local and

*Friel, A. R.: Notes on Chronic Otorrhea. William Wood & Co., New York, 1929.

systemic. The local reaction may be seen easily in certain cases. The systemic response is less in evidence but undoubtedly takes place, for if an electric current passes through the body, according to the electrical theory, it affects the entire body, since it is an integral part of the electric circuit.

The amount of zinc which will pass into the tissues is very small. Lierle was unable to find any with very delicate physical tests. However, if the laws of electrolysis are valid, the amount deposited can be calculated on the basis of known values. The ampere is defined as follows: "The unit of current shall be what is known as the international ampere, which is one-tenth of the unit of current of the centimeter-gram-second system of electromagnetic units and is the practical equivalent of the unvarying current, which when passed through a solution of nitrate of silver in accordance with standard specifications, deposits silver at the rate of one thousand one hundred and eighteen millionths (0.001118) of a gram per second." (Dawes, "Electrical Engineering," Vol. 1, p. 48. McGraw Hill Book Co., Inc. First edition, 1920.)

Assuming that the action of the electric current on silver solutions is of the same order of magnitude as on zinc solutions, then a current of one milliampere will deposit 0.000001118 grams of zinc in one second, and four milliamperes will deposit 0.000004472 grams in one second. In twenty minutes four milliamperes will deposit 0.0053664 grams (1200×0.000004472). This deposition, if it may be called such in iontophoresis, takes place over the entire surface with which the solution comes in contact. If we estimate this surface at five square centimeters, this 0.0053664 grams will be spread evenly throughout this surface. (The depth to which it penetrates is not definitely known.) This is calculated to be about 0.00147328 grams per square centimeter. Now if a small piece of tissue be removed for study, say 2.5 millimeters square, the amount of zinc in this piece will be one-sixteenth of the amount in one square centimetert, or 0.00009208 grams.

The impetus given to iontophoresis recently has led to the adaptation of several types of equipment for this work, some simple and others incorporating many conveniences. The essential features of any equipment are first, a constant and unvarying source of direct current; second, an accurate milliammeter; third, a good rheostat, which is usually inserted into the circuit as a potentiometer; fourth, a watch; and finally, the proper chemical solutions, electrodes and flexible conductors.

Dr. Dean: We will next hear from Dr. McMahon about

LATE CHANGES IN THE MUCOSA OF THE FRONTAL SINUSES AND NOSE OF DOGS FOLLOWING IONIZATION.

Dr. McMahon: From experiments made last year I concluded that definite destructive changes were brought about in the mucosa of the frontal sinuses of dogs by the ionization of a solution of zinc sulphate in the sinuses. These changes consisted of ballooning, fragmentation and complete destruction of the surface epithelium in most places, marked edema and partial disintegration of the subepithelial tissues and extravasation of free red blood cells into these tissues from greatly dilated and ruptured capillaries.

This present series of experiments was conducted in order to determine the possibility of progressive permanent changes being brought about in these tissues and in those of the nose, in nature's effort to overcome the damage which had originally been produced by ionization.

Our procedure was as follows: Healthy dogs, free from nasal infection, were selected and prepared by the intraperitoneal injection of from six to ten cc. of a solution of amytal, according to the size of the animal. The electrode used was composed of zinc, 85 per cent; tin, 10 per cent, and cadmium, 5 per cent. The solution ionized contained 8.92 grains (0.57 gm.) of zinc sulphate, 1.42 grains (0.09 gm.) of stannic chloride and 0.45 grains (0.03 gm.) of cadmium chloride per ounce (28.4 gm.). (These are the manufacturer's figures.)

The choanæ were blocked with a postnasal plug composed of a rubber finger cot filled with cotton and held in place by an attached string passed through the un-ionized side of the nose. The electrode, thinned to prevent trauma and wrapped with long fiber cotton, was carefully introduced into one side of the nose. That side was then filled with the solution so that every portion of the mucosa would be affected, as it was impossible to pack the nose completely with cotton without causing considerable trauma. The galvanic current, 2.5 milliamperes, was permitted to flow for twenty minutes, with the positive electrode in the nose and the negative electrode completing the circuit at a shaved area on the back of the neck. The dogs were killed after eighteen hours, two weeks, four weeks, seven weeks and twelve weeks, and the heads were placed in a solution of formaldehyde (10 per cent). The nasal or sinus blocks were cut after twenty-four hours, decalcified, stained with hematoxylin and eosin and sectioned serially.

Summary.—This study has shown the effects on the mucosa of the nose and frontal sinuses of dogs following ionization, the immediate widespread destructive changes and the readjustment of these delicate tissues characterized by a progressive accumulation of connective tissue in the tunica propria, as evidenced in dogs killed eighteen hours, two weeks, four weeks, seven weeks and twelve weeks, respectively, after ionization. The changes observed in the mucosa and bone of the frontal sinus are further corroboration of the reaction of such tissues to extreme irritation.

From a clinical standpoint, however, interest is centered on the changes in the mucosa of the nose. Should generalized fibrosis of the nasal mucosa be considered as an optimum state for the proper functioning of that mucosa? Increased and excessive fibrosis means depletion of the blood supply to these structures and further fibrosis; it means atrophy of the glands due to compression, as well as depression of secretions and compression of nerves, with the imminent probability of giving rise to nasal pains, hyperesthesia, neuritis and headache of a more or less intractable nature, even though there is apparently no damage to the nerve structures themselves.

All of these changes would not be expected to take place within a few months in the nose of a human being which has been ionized, as the individual reaction is too variable as to time, but there is ample reason to fear that within a comparatively short time a condition would be brought about which might be aptly termed a premature nasopause.

Whether or not it will be possible to accomplish a satisfactory clinical result by attenuated and carefully selected doses of ionization, without overstimulating tissues and inciting progressive changes which will eventually be derogatory and irreparable, remains to be seen. There should be some place in our therapeutic armamentarium for a method for which such beneficial clinical results are claimed.

The following illustrations demonstrate the changes which were brought about.

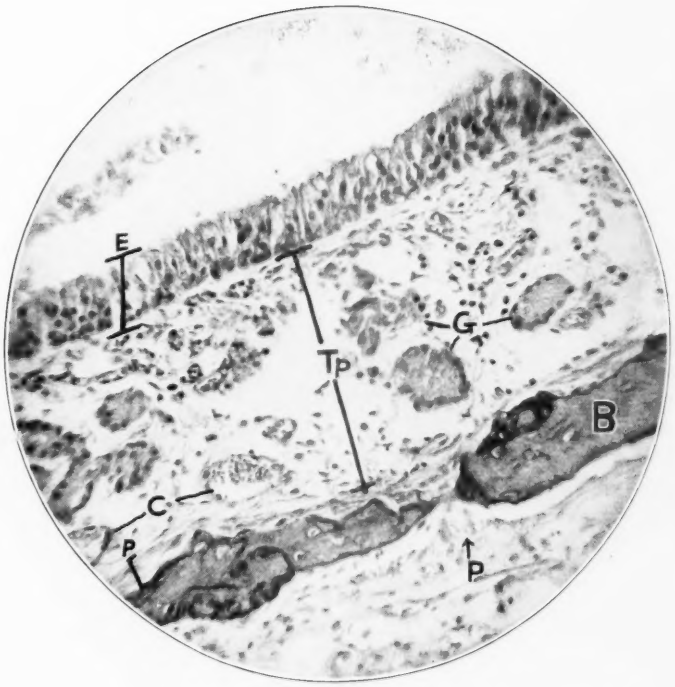

Fig. 1. Normal mucosa of the turbinate. The tunica propria has the usual number of connective tissue cells in the stroma. In figures 1 to 9—*B* indicates bone; *C*, capillary; *E*, epithelium; *F*, fibrosis; *G*, gland; *I*, ionized side; *L*, left; *N*, nerve; *P*, periosteum; *R*, right; *S*, septum; *Sp*, space; *T*, turbinate; *Tp.*, tunica propria; *U*, un-ionized side, and *X*, exudate.

Fig. 2. Mucosa of the septum and exudate shown in figure 2; high power. The exudate is closely attached to the epithelium, which is swollen and partially disintegrated. The tunica propria is markedly edematous and infiltratrated with young connective tissue cells in the subepithelial zones. The capillaries are greatly dilated, being partially ruptured. The glands are edematous.

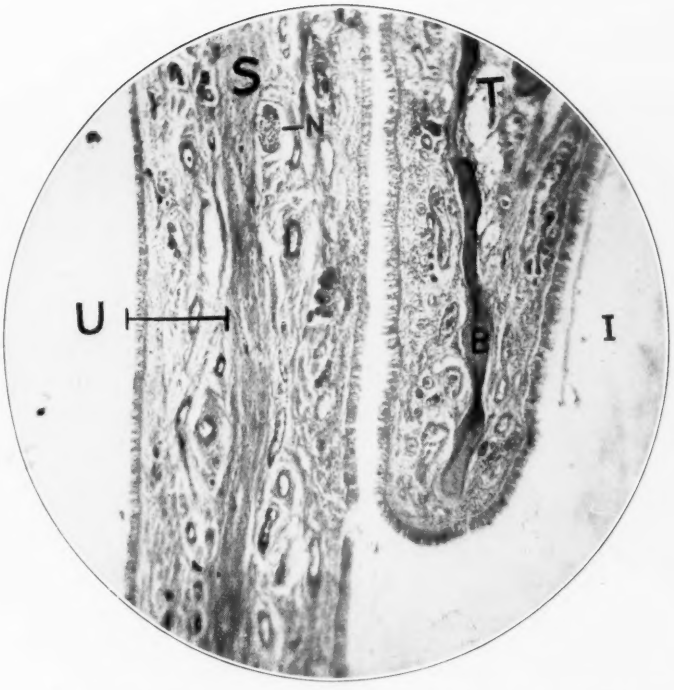

Fig. 3. Septum and turbinate two weeks after ionization. The septal cartilage is fibrosed. On the un-ionized side the epithelium and tunica propria are normal. On the ionized side the epithelium is normal and cuboidal. The tunica propria is thickened and shows early fibrosis and generalized marked round cell and young connective tissue cell infiltration in subepithelial zones. In the turbinate the epithelium is slightly thickened. The condition of the tunica propria is similar to that of the septum.

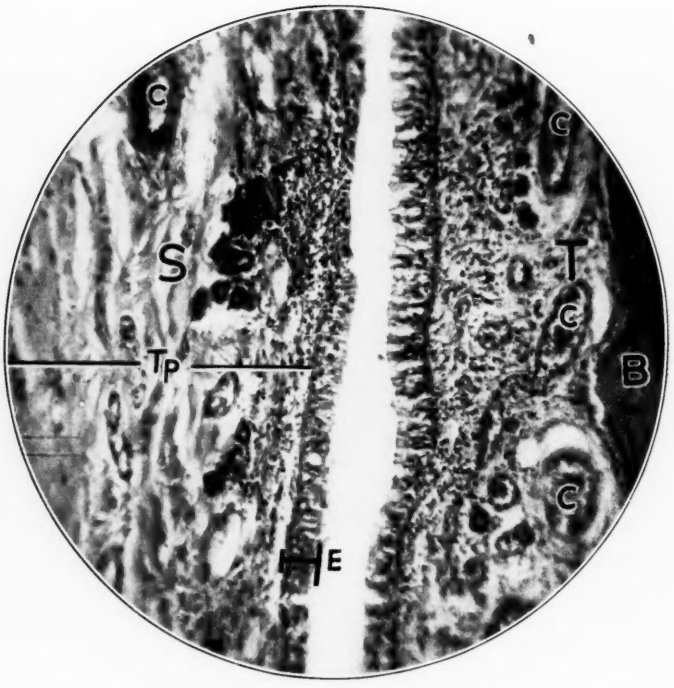

Fig. 4. Ionized side of the septum and turbinate shown in figure 4; high power. The lower two thirds of the epithelium is normal, but the upper third is cuboidal. The tunica propria shows marked round and young connective tissue cell infiltration in subepithelial zones and thickening of the connective tissue stroma in deeper portions. The epithelium of the turbinate is thickened and shows numbers of goblet cells. Cellular infiltration is marked. More advanced fibrosis of the tunica propria may be noted. The walls of the capillaries are slightly thickened.

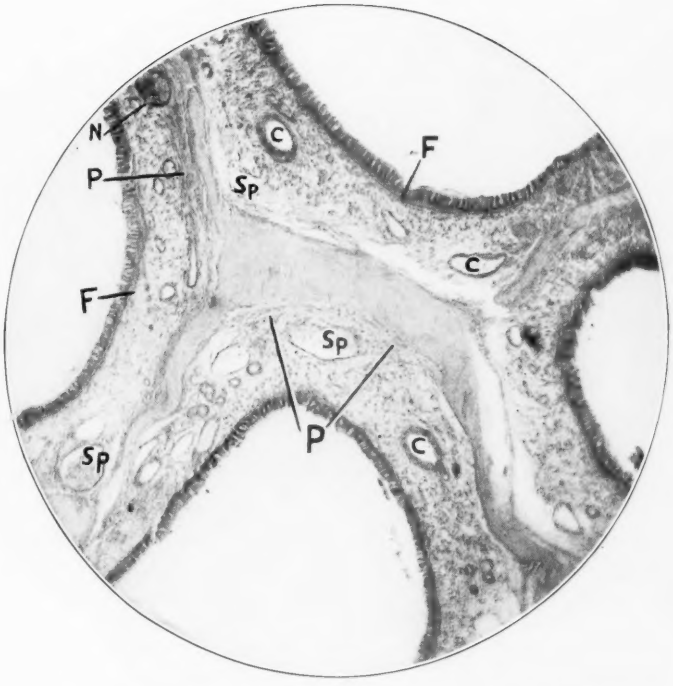

Fig. 5. Turbinate seven weeks after ionization. The epithelium is normal. The tunica propria is thickened and markedly infiltrated with older connective tissue cells. More advanced fibrosis is present immediately underneath the epithelium and adjacent to the thickened periosteum. The walls of the capillaries are thickened. Three blood spaces are indicated.

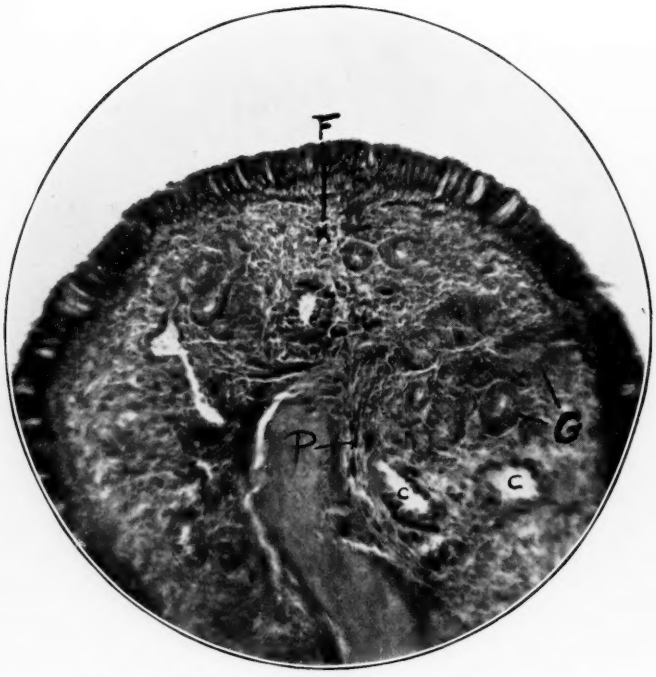

Fig. 6. High power magnification figure 5; accentuating the marked fibrosis of the tunica propria.

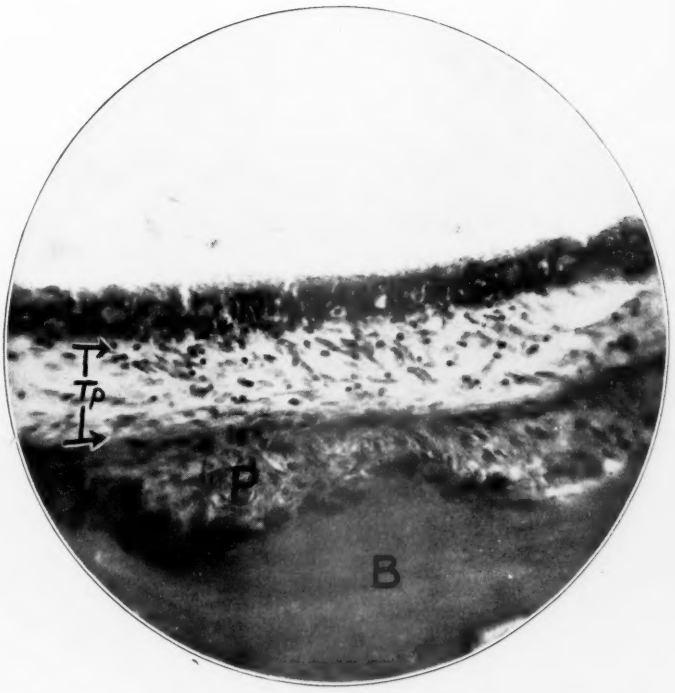

Fig. 7. Mucosa of the frontal sinus seven weeks after ionization. The epithelium is thickened and infiltrated with young connective tissue cells. Goblet cells are not present. The tunica propria is greatly thickened and markedly infiltrated with older connective tissue cells especially adjacent to the thickened periosteum.

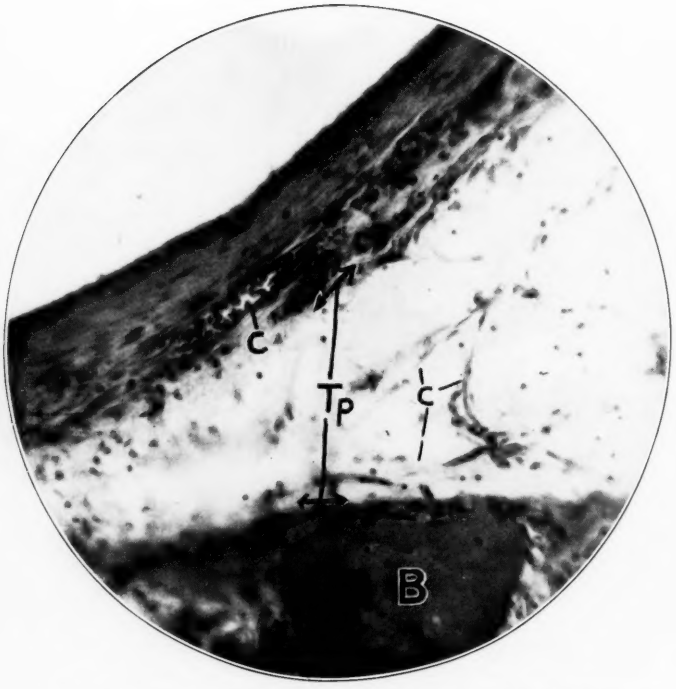

Fig. 8. Mucosa of the right frontal sinus twelve weeks after ionization. In the epithelium are now cuboidal nonciliated cells instead of the normal columnar ciliated type. The tunica propria is markedly fibrosed immediately underneath the epithelium and edematous, with many newly formed blood capillaries in deeper portions. The periosteum is thickened.

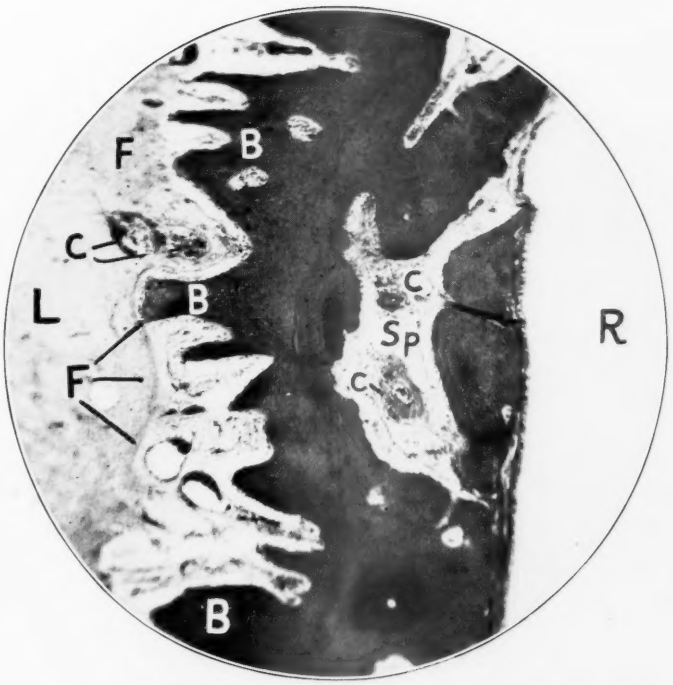

Fig. 9. Septum between the frontal sinuses twelve weeks after ionization. The epithelium of the right sinus is normal and bound closely to the bone by a dense, fibrous tunica propria. The bony trabeculae extend into the cavity of the left sinus, which is filled with young fibrous granulation tissue. Other sections show the entire sinus cavity traversed by similar bony trabeculae. There is considerable fibrous granulation tissue. The space in the bone is partly filled with fibrous tissue.

(All figures except No. 9 are reprinted from the Archives of Otolaryngology.)

Dr. Dean: The next contribution will be

PASSIVE TRANSFER RELATION OF THE REAGIN CONTENT OF THE BLOOD TO IONTOPHORESIS.

Mrs. Alexander: In working with iontophoresis, it early became apparent that when the process was applied to allergic disorders, such as hay fever and vasomotor rhinitis, in some instances there were very excellent results, and in other instances rather poor. We were considerably puzzled to account for such great discrepancies in cases which, on the suface, were quite similar.

Then we thought it might be something like this:

The mechanism underlying allergic disorders is a reaction, as probably all know—the reaction of a specific allergen with its antibody (reagin). Then, in iontophoresis, when the membrane is sloughed by the process of ionization, you would expect some of that antibody to be mechanically removed with the slough. The new membrane when it grows back would not be sensitive. The question is, can this membrane become sensitive, and how long would it take to become so? It occurred to us that if the reagin content of the blood persists, that is, if the antibody is formed in such quantity that it spills out of the tissue into the bloodstream, then the new tissue, which is formed after the ionization, would resensitize itself quite fast. If there were no reagins it would be a much different matter, and the new tissue would take a longer time to become resensitized. So we followed this idea in the clinic in the Outpatient Department.

If the patient gave any allergic history, then we performed skin tests on him, and if he gave a positive test we took serum from him, and we sought individuals for the re-transfer of this serum to the normal skin, according to the classic method of Prausnitz-Küstner.

We have a patient, "A," who gives a strong positive reaction to ragweed, say. We take some serum from that patient and put 1/10 cc. of it into the skin of a normal individual, not sensitive to ragweed, and mark the point of injection. Then, twenty-four hours later, we put in at this same spot 1/200 cc. of ragweed pollen extract. That is, we introduce the allergen to which "A" is known to be sensitive. Within five to fifteen minutes there should appear at this site a big wheal, thus showing in the blood of "A" the reagin which reacts to the allergen which has just been injected. We did this with all of our patients who came, before ionization, two weeks after ionization, three months after ionization, and we had hoped to do it for six

months after ionization, but, owing to the fact that these patients got tired and escaped us, we could not follow them that long.

Then we related our findings to the patient's own idea of the amount of relief he had obtained from iontophoresis. The original series was quite small, but the technic has since been put into the routine of the clinic.

In the original series we had twenty-five patients that we were able to follow. Of these, nine received no relief. That was a year ago. Of those nine, seven were shown to have had reagins in the blood to a high degree. Five of the original twenty-five received some degree of relief—partial relief; and of those, three were shown to have had reagins in the blood. Two did not. Eleven received complete relief; and of those eleven, the four we were able to follow for six months had no recurrence of symptoms, and two a year after had no symptoms. Of those eleven, reagins were demonstrated in the blood of only three. This was a small series, but it may be seen that certainly the indications are that the people in whose blood reagins cannot be demonstrated will have a much better chance to profit by iontophoresis. I understand that this is still largely our experience today in the clinic.

Dr. Dean: Mr. Linton will talk about

INTRAMUCOSAL TESTS BEFORE AND AFTER IONTOPHORESIS.

Mr. Linton: Intramucosal reactions vary considerably. The turbinates may become edematous and swollen, with or without injection. This is usually accompanied by an increase in nasal discharge and sneezing. Other symptoms that may accompany the nasal reaction are coughing, headache, asthma, itching of the nose, mouth, ears or throat. At times there is a feeling of stuffiness in the ears, of lacrimation or of constriction of the fauces. Nausea, rheumatic-like pains or mild pharyngitis may occur.

These tests have become a part of the routine allergic study of patients in the otolaryngologic service. It has been used to study the action of iontophoresis on the nasal mucous membrane. Alden (*Laryngoscope*, August, 1935) reported that patients that had been ionized and had received little or no benefit so far as the hay fever was concerned, gave positive mucosal reactions when ragweed extract was applied to the anterior tip of the inferior turbinate. Those securing moderate or complete relief gave no reaction.

The intramucosal tests were given before and after iontophoresis. If a patient gave a positive intramucosal reaction before ionto-

phoresis, he gave a positive intramucosal reaction after the treatment. In the following chart twelve patients were given intramucosal tests before and after iontophoresis, seven were tested only after the treatment. The reactions to the intramucosal tests after iontophoresis were similar to those obtained before. There was this difference: the swelling of the turbinates was less with those patients who obtained moderate to complete relief from symptoms following the iontophoresis. One patient gave a more severe reaction after iontophoresis using the same extract and the same dose as before.

Cases of allergic rhinitis obtaining relief from the use of iontophoresis did not react to the topical application of allergens to the nasal mucosa. Several weeks after iontophoresis in these patients who secured only slight relief from their symptoms the topical application of the allergen produced a less severe reaction following the iontophoresis than that which was produced before. It is not certain that the iontophoresis is responsible for this differenec in the reaction. It is possible that there may have existed a refractory state due to some other cause than the iontophoresis.

Name	Date of Ionization	Mucosal tests before ionization	Mucosal tests after ionization	Time in weeks after ionization	Antigen used
E. F.	R. 5- 6-35, L. 5-27-35	+	+	4	H. Dust
O. K.	R. 4- 8-35	+	+	5	Ragweed
E. M.	R. 3-16-35, L. same		+	2 & 6	Wool, ragweed
F. B.	R. 4-18-35	+	+	9	Ragweed
E. W.	R. 1-29-35, L. 2-11-35	+	+	4	Milk
A. O.	R. 5-10-35, L. 5-28-35	+	+	28	Orris root
I. K.	R. 1-25-35, L. same		+	24	Milk
S. K.	L. 4-12-35	+	+	2	Orris root
W.W.	R. 8-12-35, L. 8- 1-35	+	+	2	Ragweed
A. D.	R. 6-24-34, L. 6-24-34		+	52	Ragweed
R. P.	L. 12-11-34, L. 1-25-35		+	28	Whole wheat
R. B.	R. 8- 9-35, L. 8-17-35	+	+	6	Ragweed
C. H.	L. 8- 9-35, L. 8-15-35	+	+	11 days	Ragweed
B. E.	R. 11-18-35	+	+	8	Orris root
E. A.	R. 8- 9-35, L. 8-15-35	+	+	2	Ragweed
G. S.	R. 6-23-35, L. 6-23-35		+	48	Ragweed
H. B.	R. 7-25-34, L. 7-25-34		+	52	Ragweed
J. A.	R. 8-16-35, L. 8-16-35		+	3	Ragweed, egg
R. S.	R. 9-22-34, L. 9-22-34		+	42	Oats, house dust

Dr. Dean: Closing remarks.

The original work that has been reported by the members of the department of ear, nose and throat in this discussion represents about 50 per cent of the research work on allergic rhinitis in the Depart-

ment of Otolaryngology. The results of the remaining investigations will soon be reported.

This discussion has emphasized certain clinical phases of allergic rhinitis. The diagnosis of the nasal condition is an essential thing. Miss Zelma Alvis, working in our service, has shown that individuals having no symptoms of allergy do give positive skin tests. Many have an increased number of eosinophiles in the nasal discharge. Sometimes there is an increase in the eosinophiles of the blood. These observations will soon be reported, together with the explanation of the findings. If one of these persons had suffered from chronic intumescent rhinitis with acute exacerbations, it is easy to conceive that an erroneous diagnosis of allergic rhinitis would be made. Again, individuals with known allergic conditions, as gastro-intestinal allergy, may have at times a chronic intumescent rhinitis with an acute exacerbation and the rhinitis is not necessarily allergic.

A person may suffer from ragweed hay fever. If examined during the winter we may find skin and mucosal sensitivity to ragweed pollen, reagins in the blood stream and eosinophiles in the nasal discharge. If he has a blocked nose due to a chronic intumescent rhinitis, the latter is not necessarily allergic. It may have been caused by repeated attacks of seasonal allergic rhinitis. Nasal treatment of this condition during the winter will give a nice result until the ragweed pollen is again in the air. The nonallergic cases of chronic intumescent rhinitis do yield nicely to nasal treatment.

An understanding of a case of allergic rhinitis can only be secured after ten days of study. Skin tests should be made. Intramucosal tests are necessary in order to determine the sensitivity of the mucous membrane of the nose. Passive transfer should be done if mucosal tests are positive. In addition to this there should be a careful study made of the nose and nasal sinuses.

Dietary irregularities should be sought for. If dietary deficiencies are found the patient should be put on an optimum, well balanced diet. If because of food sensitivity essential foods are withheld, they should be replaced by things of equal value. Endocrine defects must not be overlooked. A careful bacteriologic examination is necessary. It is assumed that the examination will be preceded by a meticulous history.

The more complete an understanding we have of our patient the fewer the number of cases of severe allergic rhinitis which will be cured by nasal treatment.

As brought out in this discussion, if a person is an outstanding allergic individual, as evidenced by the presence of *plus four* reagins in the blood stream, there will be no improvement or very little improvement from any type of nasal treatment. The only benefit to be secured is that there may be a slight decrease in the obstruction accompanying the acute allergic reaction.

It has been evidenced in this discussion that treatment of allergic rhinitis is the avoidance of allergens, desensitization and nasal treatment. In addition to these things, the diet should be properly supervised, proper hygienic measures instituted and endocrine dyscrasias, if present, treated.

It is difficult to understand how one could apply a nasal treatment in an individual that has a normal nasal mucosa preceding the attack of acute allergic rhinitis. The moment, however, that we have a pathologic nose the problem becomes a different one.

Adenoids, deflected septa, exostoses, chronic purulent sinusitis, if present, should be given attention. The most important nasal condition from the clinical standpoint is a chronic intumescent rhinitis. When present the nose becomes easily blocked, either by a mild allergic rhinitis, a common cold, exposure to drafts or even by sleeping in a recumbent position. The patient often states that the side of his nose on which he lies is blocked. Chronic intumescent rhinitis is caused by acute attacks of allergic rhinitis, by repeated attacks of common cold, by irritating gases, dusts, etc.

It is this condition which is so beneficially affected by iontophoresis. Iontophoresis will shrink the moist, boggy mucosa of the nose and leave a membrane which is thinner and dryer. If a patient with chronic intumescent rhinitis has one side of the nose treated by iontophoresis and several weeks later develops a common cold the treated side remains dry; the mucous membrane is pale; there is no nasal obstruction. The untreated side is blocked, reddened and has the usual abundant watery discharge. Iontophoresis will produce a thinning and dryness of the normal mucosa. It benefits the patient by interfering with the swelling of the membrane during an attack of allergic rhinitis, common cold, when lying down, sitting in a draft, etc.

The influence of iontophoresis on the tissues of the nose, including the end organs of the parasympathetic system, have been described. It is most unlikely that iontophoresis has any effect on the allergic reactions of the tissues themselves. Because of the changes

in the tissues some of the disturbing features of acute allergic rhinitis are lost. The ability of the nasal mucosa to absorb inhaled pollens seems to be disturbed. At any rate, contact application of pollen to the nasal mucosa usually does not produce as much reaction after iontophoresis as before, particularly in patients whose hay fever is benefited by iontophoresis. The normal nasal mucous membrane does absorb pollens; the treated membrane is more like the skin and resists the entrance of the pollens into the tissues.

There is no evidence whatsoever that iontophoresis influences the allergic status of the nasal mucosa or of the organism as a whole. The reactions of the nasal mucosa to the intramucosal tests are not changed except that the membrane does not swell so much.

Persons who have been treated by iontophoresis for over a year and have gone through a siege of hay fever do have a return of the edema of the tissue. In nonallergic rhinitis the results of the iontophoresis are more permanent.

Nine months ago we reported the following iontophoresis of three patients, in two instances the blurring of the maxillary sinus was improved, while in the third there was no change. It is probable that the decrease in the thickening of the lining membrane was a coincidence. We have not been able to confirm this observation in cases studied later. The lining of the maxillary sinus of a guinea pig, taken eight days after iontophoresis, showed no change. An ethmoid cell in the middle turbinate, studied three months after iontophoresis of the nose showed no change. On the other hand, the one case of ozena that appeared after this treatment had a typical foreign body odor. Washing a little débris out of the maxillary sinus permanently controlled this condition.

In chronic intumescent rhinitis one can often secure just as good a clinical result as by iontophoresis by using procedures that do not cause the deleterious results that we get with iontophoresis. The chronic intumescent membrane may be made quite normal by the avoidance of offending allergens, by desensitization, by the removal of adenoids or by a proper diet combined with the use of a vaccine. Patients who have suffered from nasal stoppage for ten years have secured complete relief by the avoidance of allergens, and the nasal mucosa has returned to an almost normal condition. One patient who suffered from a nasal stoppage had a bilateral Caldwell-Luc operation performed several years ago without benefit; later the patient was treated by iontophoresis, without improvement, but did secure relief

from the administration of a proper diet plus vaccine and toxic filtrates.

It is axiomatic that iontophoresis should be used only after it has been proven that a satisfactory result cannot be secured by more simple procedures.

The treatment of acute allergic rhinitis is, first, the avoidance of allergens and desensitization. If a co-existent chronic intumescent rhinitis cannot be controlled by simpler procedures we should be certain that the beneficial effects of iontophoresis will outweigh its deleterious action.

IX.

OTOSCLEROSIS

A RÉSUMÉ OF THE LITERATURE FROM 1928-1935

Issued by the Central Bureau of Research

of

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INTRODUCTION.

The literature on otosclerosis has been so extensive during the past eight years and so much of importance has been contributed that the Central Bureau of Research of the American Otological Society decided it would be inadvisable to republish contributions in full in this volume. Moreover, stringent financial conditions made such a decision imperative.

Included in the index are the names of authors receiving grants from the Central Bureau, although the work of a few of these authors does not appear to bear directly upon otosclerosis.

The material has been arranged under headings according to the various phases or departments of theory, fact and experience. It is to be distinctly borne in mind that the quotations and opinions in this book are wholly those of the authors quoted. In no instance does the translator or the editor endorse or condemn any opinion, no matter how sound or how fantastic it may appear.

After each author's name in the text is given the year of the publication quoted, so that in the annotated index under the author's name the complete bibliographical data may be obtained. In the annotated index will be found a cross-reference indicating by numeral the section in which the author is quoted.

Both the text and the annotated bibliography have been written and prepared for publication by Dr. F. Robbins.

The work has been supervised and edited by Dr. Edmund P. Fowler. ARTHUR B. DUEL, M.D.

This review of the literature from 1928 to 1935, inclusive, constitutes Otosclerosis, Vol. III, issued by the Central Bureau of Research of the American Otological Society, Inc. None of the literature is published in full.

Co-operation with the ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY has made it possible to publish the text in the March issue and the annotated index in the June issue of this journal. This arrangement conserves the research fund and assures a much wider distribution than would otherwise have been possible. It is hoped it will serve to interest and enlist many in the work for a better understanding of Otosclerosis and other lesions causing progressive deafness. EDMUND P. FOWLER, M. D.

I. HEREDITY.

Abnormal heredities, according to Bauer and Stein (1925), originate through so-called germ variation or idiokinesis, namely, through alteration of one or more genes, under the influence of some harmful factor acting upon the parental organism. In their article on endocrinic affections of the auditory organ (1926), they point out that a positively established fact in the etiology of otosclerosis, as well as progressive labyrinthine hardness of hearing, is not some anomaly in one or several endocrinic glands, but rather the hereditary constitutional disposition, transmissible through the germ plasm. It is readily understood that such a constitutional disposition can be inherited also, when the most careful investigations of the family in so far as practicable, fail to reveal an analogous affection. In view of the existence of a recessive heredity furnishing the constitutional disposition to otosclerosis, as shown by these writers, no larger percentage of a demonstrably transmitted faulty heredity is to be expected than has been actually established by all observers.

Otosclerosis is included, by Schwarz (1933), under the heading of hereditary ear diseases, and its transmission to part of the offspring is generally conceded. The study of heredity in otosclerosis is made difficult through the uncertainty of the diagnosis in many cases, especially in members of the tainted family who have not been carefully examined by a specialist. A small otosclerotic focus does not necessarily give rise to appreciable deafness; consequently, some members of a given family may have otosclerosis without indications of the disease in the history. Such is probably the case when the diagnosis of otosclerosis is rendered in only a few members of a family with a faulty heredity or when a generation seems to have escaped entirely. The peculiar character of the disease with its variegated functional disturbance accounts for the difficulty of the diagnosis, which cannot always be positively rendered. The characteristic sign is the disturbance of sound conduction, with its distinctly negative Rinne test and the remarkably prolonged Schwabach test. The presence of otosclerosis is probable when normal findings are noted in the tympanic membrane, the middle ear and the tube, and when a normal mastoid process is also demonstrable. Occasionally, the otosclerotic focus which is usually bilaterally situated, can likewise be directly recognized by a reddish blush of the posterior upper portion of the tympanic membrane.

Among the transmissible diseases of the ear, a distinction must be made between otosclerosis and middle ear deafness as the result

of chronic affection due to a congenital inferiority of the mucosa. The frequency, course and degree of this most common form of middle ear deafness have been shown by genealogic investigations to be dependent not only upon the mode of infection, but also upon the constitutional-congenital susceptibility and upon the constitutional-congenital power of defense and reaction of the mucosa.

As pointed out by Goerke (1932), the existence of a disease in the ascendency and its frequent familial occurrence are not to be considered as a proof of hereditary transmission, for in recessive sequences eventual bearers of stigmata may be missing in the entire accessible ascendency, while, on the other hand, an increased manifestation in a given family may occur also in diseases caused by environmental conditions. Nor may a proof of hereditary causation be accepted in the fact that the disease was present at birth or developed in the first few years of life; for there exist ailments acquired during intra-uterine existence or due to birth injuries, namely, congenital but not inherited diseases, and on the other hand, the onset of well-marked and undoubtedly hereditary diseases may be delayed until relatively late in life. With special reference to ear diseases, a study of the behavior of the vestibular and cochlear nerve is of great importance in this connection. The simultaneous presence of other signs of degeneration, such as osteogenesis imperfecta, osteoporosis, osteitis deformans, and so forth, is suggestive of faulty heredity in the case of the ear disease. The foregoing statements, although rendered with regard to deafmutism, are equally applicable in otosclerosis, another degenerative process.

Heredity as an etiologic factor in otosclerosis, with its variegated modalities and intrinsic difficulties, has been extensively discussed in Otosclerosis, Volume I, Section 2. No repetition of old or enumeration of new pedigrees and family trees is here contemplated, as the essential facts have not changed, although great-grandparents have long departed and great-grandchildren have taken up their infirmities. An instructive study of the hearing of children in families in which both parents had otosclerosis, was presented by Davenport, at the meeting of the American Otological Society in 1930. The axiom that simple recessive traits, when they occur in both parents, appear in all of the offspring, was very closely confirmed in the seven investigated families. Only in the first family, one of eight children remained unaffected and survived to the age of sixty-three years. Ninety family charts, including forty-eight from their original records, the remainder from the literature, were contributed by Davenport, Milles and Frink (1933), in their article entitled "The Genetic

Factor in Otosclerosis." They incline to the assumption that otosclerosis develops under external conditions favoring it, whenever the individual shows a combination of two dominant hereditary factors: A factor *X* that lies in the sex chromosomes, and a factor *A*, that lies in one of the autosomes. The hypothesis is suggested that the autosomal gene modifies the reaction of the mesenchyme, especially the osteoclasts and osteoblasts; the sex-linked gene acts differentially between the sexes, possibly affecting the calcium metabolism.

A study of the family history of 106 cases of otosclerosis from Uffenorde's Clinic in Marburg, was reported by E. Schmidt (1933), in Germany. A definite family history of deafness was obtained in fifty-seven cases, but in ten of these cases it remained doubtful if the deafness was otosclerotic or senile in character. Heredity evidently plays an important etiologic part in at least half the cases of otosclerosis. Likewise, in 50 per cent of the cases, pregnancy was shown to exert an unfavorable effect on the evolution of otosclerosis; twenty-five of forty-nine women who had been pregnant one or more times had undergone a well-marked diminution in hearing. Twenty-four of the studied women had noticed no change in their hearing faculty during pregnancy or in the puerperium. Three instructive family charts are published by Schmidt (1933): One of these charts starts with a woman suffering from otosclerosis, who had a son with otosclerosis (second generation); he married a normal woman; of their eight children, three girls had otosclerosis (third generation). Two other children became deaf in old age; the others were normal. One of the otosclerotic girls of the third generation married a man who had normal hearing but whose mother and sister were both otosclerotic. Three of their four children had otosclerosis (fourth generation), and one of these became totally deaf. No other cases of otosclerosis appeared in the fourth generation, although the members of the third generation had one or more children. The normal sister of the three otosclerotics of the fourth generation had four children, none of whom have shown signs of otosclerosis, at ages of fifteen to twenty-four years, at the time of the report.

Otosclerosis is included by Hammerschlag (1932) under the heading of acoustic heredopathy, a unit from the biologic viewpoint but clinically distinct in its manifestations and time of onset. In addition to the changes in the auditory nerve apparatus and the membranous labyrinth—its supporting tissue—otosclerosis presents a second hereditary factor, in the form of the focal alterations in the bony labyrinth capsule. While the otosclerotic foci at the site of predilection, the oval window, with superadded stapes ankylosis, give

rise clinically to deafness of the conduction type or middle ear type, the foci situated at other sites in the capsule result in deafness of the internal ear type. Otosclerosis, in Hammerschlag's opinion, is undoubtedly closely connected with hereditary degenerative (constitutional) deafness, in which otosclerotic changes in the labyrinth capsule are not uncommon. Moreover, the two types of deafness are known to occur together in certain families.

Otosclerotic foci which leave the window region intact and are situated within the bone of the labyrinth capsule, thus giving rise to no clinical manifestations, are of importance for the student of heredity, because a recessive heredity can be simulated, as pointed out by Weber (1934) when the typical clinical signs are missing and the otosclerosis has its site in the labyrinth capsule. He cautions that for prophylactic purposes marriage between two persons of otosclerotic families must be discountenanced, not only those with signs of faulty heredity, but as well of the others, because the latter are carriers of the recessive hereditary factors.

On the basis of his study of otosclerosis, Warwick (1931) arrives at the conclusion that the so-called heredity tendency to otosclerosis results from a deficiency in the formation of the temporal bone in fetal life and early infancy. This developmental deficiency is surmised to induce a sensitization of the cartilage cells in adult life, rendering them responsive to changes in the hydrogen ion concentration of the blood and blood calcium such as occur in various forms of endocrinic insufficiency.

A "synthetic review" of the entire subject of hereditary transmission of psychic or somatic characteristics from progenitors to offspring was offered by Maffeo (1930), who makes a distinction between "auricular sclerosis" and "otosclerosis." The former, or chronic catarrhal otitis media, is due to propagation to the tympanum of catarrhal lesions of the upper air passages by way of the eustachian tube. In otosclerosis, from the histologic viewpoint, the fundamental lesion consists in the presence of diseased osseous foci in the substance of the labyrinth capsule, these foci having their seat of predilection at the oval window, secondarily giving rise to stapes ankylosis. Gradenigo (1924), one of the first and most thorough students of the modality of evolution of progressive deafness in connection with heredity, stated on the basis of his study of 132 genealogic trees of patients, comprising from three to four and up to five successive generations, that consanguinity of the progenitors, always conceded to have a great influence on the development of diseases of recessive

type, apparently does not induce in the direct descendants a demonstrable increase in the number of patients with otosclerosis. As the result of more extensive investigations, the recognition of otosclerosis as a familial disease, and as such transmissible to future generations, according to the Mendelian type, may be confidently anticipated. The familial diseases manifest themselves by a definite mode of affection of a special organ or system. As a rule, they attack several members of the same family and are repeated in this family in successive generations. In the afflicted family they present a practically identical course and symptomatology in each of the affected individuals. The alterations nearly always show a tendency to manifest themselves in a definite organ and at a definite time of life. Although distinctly transmitted through heredity, they are often subject to the influence of external injurious factors. The anatomic basis of the affected organ or system is abnormally developed in all these cases. Extensive investigations will assuredly permit the recognition of otosclerosis as a familial disease and as such transmissible to future generations, in conformity with the Mendelian law.

Deafness as a eugenic problem was studied by Tinkle (1933) in the family histories of thirty-eight cases of otosclerosis. (On file at the Ohio State University.) He states that the hypothesis of a single pair of recessive genes is sufficient to account for all the data noted by him in his own work or the findings of other investigators on the heredity of otosclerosis.

The following observation is of considerable interest from the viewpoints of eugenics, heredity and prevention: Grabscheid (1935), at a meeting of the Austrian Otological Society, Vienna (October, 1934), presented a case of unilateral (?) otosclerosis, with aggravation of the hearing capacity after the seventh pregnancy. The patient was a woman, 54 years of age, who had undergone the radical operation on the left maxillary antrum at the age of 27 years; immediately afterwards, left-sided aural tinnitus and hardness of hearing supervened. At the age of 42 years, this woman suffered an apoplectic stroke. She gave a gynecologic history of four deliveries and six abortions. Six pregnancies remained without influence upon the hardness of hearing, until in the puerperium of the third childbirth (seventh pregnancy) a considerable aggravation of the left-sided hardness of hearing occurred and became worse after the apoplectic stroke. Among the patient's four living children, the second and third child show otosclerosis. In the case of the second child, the signs of otosclerosis are demonstrable on the left side, while in the third child, the otosclerosis is bilateral.

Otosclerosis in identical twins was recently described by Shambaugh (1935). According to his study of the literature, this comparatively rare occurrence has been observed a total of five times. Otosclerosis in identical twins offers a unique opportunity to study the etiology of this common disease. Twice the disturbance began five years earlier in the twin who was more susceptible to head colds. Once the deafness began ten years earlier in one twin than in the other, and here the most likely cause for the striking difference was the much greater susceptibility to head colds; and further, the progress of the deafness in this patient was most rapid at a time when she was having many colds and was much slower when she became less susceptible to colds. This would appear to be in conformity with the contention of Fowler (1933) that the large proportion of otosclerotics show signs of prior inflammatory episodes in the middle ear and nasal sinuses.

II. EMBRYOLOGY.

The development of the labyrinth capsule and the oval window is described in Otosclerosis (1928), in the chapter on congenital conditions of the labyrinth capsule. In the normal newborn, the enchondral capsule has been shown (Weber, 1930) to consist of marrow spaces and cartilage remnants, and of a lamellar bone that has become deposited on the cartilage. The cells of the lamellar bone are arranged in the longitudinal axis of the lamellæ. The lamellæ themselves pass essentially parallel to the surface of the labyrinth. A marrow space is found in the center of the entire enchondral capsule. Usually the marrow spaces at the time of birth are already extensively restricted through deposition of lamellar bone on the cartilage remnants, and are subdivided by spongiosa-like septa. The periosteal capsule of the normal newborn consists of plexus-like bone which under the periosteum is further strengthened through new layers. The normal tissue of plexus-like bone encloses only relatively small marrow spaces. The ground substance of this bone is homogeneous; the bone cells are irregularly arranged. At the time of birth, no formation of lamellar bone has as yet occurred in the external capsule. The petrous bone differs essentially from all other bones in the preservation of chondroid supporting tissue in its interior until an advanced age, due to the early conclusion of its development; furthermore, all the characteristics of the infantile bone are likewise preserved until an advanced age. Inferiority of the petrous bone, predisposing to otosclerotic disease, is transmitted to the offspring, as well as general inferiority of the organism. The onset of otosclerosis requires a superadded pathologic factor, presumably in the form of some metabolic disturbance. (Weber, 1930.)

The "capsular bone" (temporal bone), unlike other bones, as shown by Bast (1930), originates from various ossifying segments. Islands of calcified cartilage tissue persist and are sometimes still demonstrable in the adult. The foci of ossification originate in different periods of embryonic life. Considerable difference in the degree of ossification was observed in the capsular bones of human embryos. No less than fourteen centers of ossification were demonstrated. To begin with, a tiny island situated at the first cochlear convolution, appears in the sixteenth week. The fourteenth and last focus is situated at the posterior branch of the sagittal semicircular canal. In the twenty-sixth week ossification terminates in the region around the base of the stapes. The petrous bone differs in its devel-

opment from other bones of the body in that there is here no absorption of the primary bone followed by the appearance of a secondary lamellar bone. It is noteworthy that the starting points of otosclerosis correspond with the most common sites of remnants of embryonic tissue. The bony capsule in the fetus was shown by Bast (1930) to develop from the cartilage capsule that precedes it; the ossification not beginning uniformly throughout the capsule, but at certain definite points or ossification centers. The bone of the periotic capsule is of three types: (1) Perichondral or periosteal bone, formed from the cambium layer of the periosteum or perichondrium around the cartilaginous capsule, of the same type as perichondral or periosteal bone in the long bones. (2) Enchondral bone formed in membrane as the perichondrial bone, but around the remaining cartilage islands in the spaces that were filled with cartilage previous to their excavation by the osteogenetic buds. This primary endochondral bone does not differ from primary endochondral bone in other parts of the body, but in the otic capsule it remains as such, while in other parts of the body it is usually removed and replaced by secondary or Haversian bone. (3) Intrachondral bone, or calcified cartilage, usually referred to as cartilage islands or interglobular spaces. These cartilage islands are now interpreted by both Brühl (1930) and O. Mayer (1930) as calcified cartilage, in which cartilage cells are replaced by bone cells. Complete ossification of the capsule is delayed until after birth or indefinitely, and around the fissula ante fenestram, or Cozzolino's zone, the otic capsule remains cartilaginous until after birth and sometimes throughout life. Special interest in this respect is attached, pathologically and clinically, to the region around the footplate of the stapes, on account of the frequent localization of otosclerotic foci in this part of the capsule. According to later studies of Bast (1933) on the development of the otic capsule, more particularly the fissula ante fenestram, and its relation to otosclerosis, the anterior end of the fissula is an "outpouching" from the periotic tissue and develops in a similar manner, both arising from precartilage which undergoes a regressive change to form a vacuolated reticular tissue. Through the entrance of blood vessels from the side of the capsule near the middle ear, tissue growth is stimulated and at the center of the fissula a loose reticulated, vascular connective tissue is formed in the fetus. At the periphery of the fissula, the new formed fine fibrillar connective tissue changes into cartilage. Bast points out that the otosclerotic process, although often beginning in the region of the fissula, does not as a rule first attack the tissue of the fissula or even the cartilage islands, but rather the surrounding bone. On the basis of his findings in animals, Bast

does not agree with Guggenheim (1931) in that the fissula ante fenestram in man represents a rudimentary structure. (Guggenheim believes that the fissula is a homologue of the accessory endolymph duct of the spine shark, the thorn ray and the frog.)

Leiri's studies (1931) of the cartilage formations of the labyrinth capsule in human embryos at different ages demonstrated the presence of persistent cartilage in front of the oval window at a very early embryonic stage, prior to the appearance of blood vessels in the labyrinth capsule. Most of the cartilage was avascular in a five months' fetus, and in a six months' specimen no blood vessels were found in this cartilage. The cells here are smaller and the connective tissue fibers are finer than in the vascular cartilage formation in the region of the semicircular canals, where the cartilage canals disappear on completion of the process of bone formation, whereas the cartilage in front of the oval window has repeatedly been shown to persist in numerous cases.

The site of predilection of otosclerotic foci has been shown by pathologic investigations to be in the cartilage "growth zones," especially in front of the oval window, where one of these embryonic cartilage formations often persists more or less indefinitely. As so-called growth zones in the embryonic development of the capsule have been shown to correspond to the epiphyseal lines and articular cartilages in the development of the long bones, Leiri (1931) claims a similarity in the factors back of the pathological changes in otosclerosis and in juvenile epiphyseal disturbances (osteochondritis deformans juvenilis): namely, the presence of cartilage growth zones and the action of mechanical strain. The constant mechanical strain to which the labyrinth capsule is exposed—due to the tension of the basal membrane, the movements of the stapes and the membrane of the round window, induced by sounds—has been repeatedly emphasized by him (1929). The pathologic changes of otosclerosis presumably begin in early life, and characteristic foci have been found in young children. After the age of two years the ossification of the capsule is complete. Otosclerotic changes, according to Guild (1930), may begin as early as the end of the first year of life, a much earlier age than heretofore demonstrated.

The resorption of the cartilage in the canal portion of the otic capsule in the human fetus was investigated by Bast (1932) on the basis of serial ear sections of fifty-two human fetuses from eight weeks of age to full term. The growth of the semicircular canals was shown to take place within a mass of cartilage, situated around, between and within the arcs of the semicircular canals. The expansion

of the canals involves an extensive destruction of cartilage between and within the arcs of the canals by necrosis and connective tissue ingrowth. The semicircular canals reach their approximate maximum growth at about half term or when their capsule begins to ossify. The vascular buds penetrating into the connective tissue become ossified from advancing ossification centers, but do not initiate ossification. The cartilage growth between and within the arcs of the canals is reduced to a minimum by the process of vascularization.

Cartilage Remnants.—The arrangement and distribution of the cartilage remnants (cartilaginous interglobular spaces) in the human labyrinth capsule were studied by Steinberg (1933) in forty specimens which showed a great irregularity in their behavior. But a very close similarity in the number and arrangement of the cartilage remnants was found in capsule specimens from the right and left side of the same individual. No variation in the number of the cartilage remnants according to age was noted in twelve specimens derived from persons between three and eighty-three years of age. The largest number of such remnants occurred in specimens derived from the deeper portions of the capsule. In no series were more or even as many cartilage remnants found in the region of the upper semicircular canal than about the oval and round window. In most cases numerous cartilage remnants were found in the bony capsule between the cochlea, the oval window and the internal auditory canal, extending from the cochlea on the one side and the internal auditory canal on the other side, and from there to the niche of the oval window. In this set of specimens more cartilage remnants were found at the round window and the lower ampulla than in any other region of the capsule. The cartilage remnants here extended from the ampulla to the niche of the round window on the one side and from the posterior portion of the basal coil of the cochlea on the other.

So-called persistent cartilage remnants in the domain of the bony labyrinth capsule were described by Altmann (1932) in a girl of two days, in a six months' male fetus, and in a seven months' female fetus, all with congenital malformations of the external ear. In the first case this remnant was found in the middle layer of the labyrinth capsule, invading the outer periosteal layer. To the observer's knowledge no cartilage remnant has ever before been noted in this particular location.

From a study of the development of the oval and round windows, in lower animals and in man, Bonain (1930) learned that

the oval window is present in rudimentary form in the lower orders before the labyrinthine organ of hearing is developed and that its purpose is to protect the static labyrinth. The round window, which serves for the transmission of the sound waves, is not developed until the labyrinthine organ of hearing is present. The oval window and the chain of ossicles are designed rather to protect the labyrinth and regulate the transmission of sound waves. Stapes ankylosis, or even absence of the stapes and other ossicles, thus does not induce severe deafness but lessens the hearing for certain sounds, especially low tones; not so much for the voice sound. This explains, in Bonain's opinion, the insidious onset of otosclerosis, its slow progress and the occasional appearance of tinnitus before the deafness is noticeable. The initial lesion is apt to be situated in the region of the oval window, and even in the presence of stapes ankylosis deafness is not pronounced and does not become rapidly progressive before the involvement of the round window. Loss of hearing for the low tones, one of the characteristic symptoms of otosclerosis, is the result of involvement of the stapes and oval window.

Otosclerotic foci which leave the window region free and are situated in the midst of the bone of the labyrinth capsule, thus giving rise to no clinical manifestation, are of importance for the student of heredity and eugenics, because a recessive heredity is simulated (M. Weber, 1930). Imperfections of the mesenchyma are held responsible for the premature transformation of the labyrinth capsule, a process which according to the normal standard is delayed until a very advanced age.

III. REGRESSION.

The underlying cause of otosclerosis—as propounded by Guggenheim (1931-32-33-34)—is mesenchymal and embryonic, or supervenes soon after the fetal period. The typical changes have been shown by him in a seven months' fetus (1933). He originates and, in his book (1935), maintains the regression theory of otosclerosis, namely, that the persisting mesenchymal cells retain a potentiality for differentiation and that in otosclerosis they are activated by the regressive trait of forming a capsule as it is found in lower vertebrates with no oval or round window. The development of the otic capsule is traced by Guggenheim from the beginning of ossification (in the sixteenth week of embryonic life) to its completion. He emphasizes that the mammalian ear, including the human ear, "in its ontogenesis passes through the stages of phylogenesis." His phylogenetic studies have shown that the two labyrinth windows, oval and round, and the cochlea, are relatively new structures. When the genes of the lower vertebrates are present in human ear capsules and attempt to express themselves, the natural tendency is toward the construction of an ear of the lowest vertebrate type. The result is an "attack" upon the oval window, less frequently upon the cochlea and round window, and very infrequently upon the canal region.

Otic capsules without windows and with only utriculus and canals are found in certain lower vertebrates; and "phylogenetically there was probably a period when oval window, round window, cochlea and sacculus had not evolved." All persisting undifferentiated mesenchyma cells throughout the capsule of predisposed individuals probably contain "the genes of regression," and may therefore form an otosclerotic focus, unless inhibited sufficiently by normal genes. In the latter circumstances, transmission of the genes of regression to the offspring is possible. The pathologic changes of otosclerosis, contrary to the former assumption of its onset at puberty or later, have recently been found in young children and even prior to birth. Serial sections, of a two months' embryo from a typically otosclerotic mother, will show, he hopes, in the precartilage stage, something that will throw further light on the problem.

In an earlier contribution on the phylogenesis and ontogenesis of the footplate of the stapes (1931), Guggenheim had already raised the question, if, in view of certain facts pointed out by him, otosclerosis should not be regarded as a regression rather than a disease

process. The site of predilection in otosclerosis is anterior to the oval window, the location of the fissula ante fenestram, a structure present in all human embryos and usually persisting throughout life. High magnification of the normal fissula shows a heavy cartilage wall, and with oil immersion it is seen to contain many pluripotential undifferentiated mesenchymal cells and other elements. If these mesenchymal cells contain the genes of lower vertebrates, otosclerosis may develop. The marrow spaces of normal as well as otosclerotic labyrinth capsules also contain pluripotential undifferentiated mesenchymal cells, and the proliferation of such cells containing the genes of regression induces pressure on the surrounding bones with the pathologic changes characteristic of otosclerosis. In the region of the annular ligament, posteriorly and anteriorly, there is a plate of cartilage over the footplate of the stapes and over the capsule, which is sensitive to mesenchymal attack. In typical otosclerosis the focus anterior to the footplate of the stapes sends out "myriads" of mesenchymal cells. resulting first in resorption, then in the formation of otosclerotic bone in the footplate; the ligament is obliterated by calcium deposit, and thus the capsule is closed: regression to a lower vertebrate form.

All of Guggenheim's points were illustrated by him, with slides, in a lecture addressed to the New York Academy of Medicine, December 20, 1933, entitled "The Regression Theory of Otosclerosis." The Transactions of the American Otological Society, Volume 23, 1933, bring his contribution from the Oscar Johnson Institute, Washington University, entitled "Otosclerosis: a Regression?" Discussion by J. Gordon Wilson and other leading otologists. The lecturer emphasized the outstanding characteristics of otosclerosis, as: First, the condition is hereditary, with a genetic formula of two dominant factors, one sex-linked. Second, otosclerosis is usually bilateral and very frequently bilaterally symmetrical. Third, there is a site of predilection, anterior to the oval window, in the region of the fissula ante fenestram. Next, the three structures which are usually involved, the oval window, the round window and the cochlea, are recently acquired structures; and next, otosclerosis may involve the footplate of the stapes, but it does not involve the crura (derived from the second hyoid arch). The footplate—according to him derived from the labyrinth capsule—returns, in otosclerosis, to the tissue whence it was derived. To quote Guggenheim's words: "We believe otosclerosis is a variation in these structures (recently acquired: oval window, round window, cochlea), not accidental, but due to the presence of genes of regression." "We believe that it is

possible that otosclerosis is due to the presence in the human ear of fish genes, which produce a secondary activity after the genes for normal structure have expressed themselves, and that the lower vertebrate genes express themselves secondarily by the production of this web bone in an attempt to form a capsule of their own period." "The genes that produce otosclerosis, we believe, originated in the fish period."

An objection to the regression theory is conceded by its originator: No other instance in the human body has been found in which a tissue has reached normal development and then shown regression.

The literature does not yet contain expressions of many opinions on the theory propounded by Guggenheim. Gottlieb, in 1934, writes as follows: "Recently the regressive theory of otosclerosis was presented to the otologic world. This theoretical structure is erected upon a very insecure foundation. It is based upon the finding of bony lesions similar to those found in otosclerosis in the otic capsule of a fetus of seven months. A parallel is drawn between the finding of a closure of a preformed oval window in the herring and other fishes and the ankylosis of the stapes and the obliteration of the round window in cases of otosclerosis. In the cases of the herring and the sturgeon the obliteration of the preformed window is accomplished with normal bone and cartilage. The otosclerotic lesion is distinctly pathologic. It is contended that in otosclerosis there is a reversion on the part of the human labyrinthine capsule to the fish stage."

Lewy, in 1934, mentions his own experimental findings (calcium fluoride feeding of white mice) as opposed to the regression theory of Guggenheim, "who would trace the origin of otosclerosis to genes originating in the ancient ancestry of Proteus anginas."

In the discussion of the startling theory propounded by Guggenheim in his lecture before the New York Academy of Medicine (1933), it was pointed out by J. Gordon Wilson, with respect to the fissula as an alleged vestigial organ, corresponding to a structure found in certain fish, that no trace of the fissula has been found, in birds or mammals, outside of man; that is a risky procedure to point to a structure in a low vertebrate form as the predecessor or homologues of the fissula, without explaining what happened to it or why it disappeared during the million odd years which intervened between the appearance of fish and the advent of man.

In his recently published book on Otosclerosis (1935) the ear disease known under this name is discussed and explained on the basis of Guggenheim's theory of regression. The author contributes chapters on the development of the ear in man and on the pathogenesis of otosclerosis.

IV. BONE PATHOLOGY.

Otosclerosis as a Bone Disease.—The diseases of the osseous system and their manifestations in the human otic capsule form the subject of an extensive study by Nager and Meyer (1932), who on the basis of their findings maintain that otosclerosis belongs to the group of osteodystrophies. The experience that similar changes have been produced in bones by various experimental procedures suggests that the bone changes observed in the osteodystrophies, including otosclerosis, are not due to any specific cause, but represent a general reaction of bone tissue to various metabolic disturbances. Certain distinctive histologic features are dependent upon the localization and slow development of the ear disease. The foregoing extensive bone studies have shown the fundamental histologic conformity of osteitis fibrosa Recklinghausen and osteitis deformans Paget on the one hand and otosclerosis on the other. The otosclerotic changes of the labyrinth capsule can now be readily grouped under the heading of the osteoses or osteodystrophies. The general bone reaction to different irritant factors indicates a histologically nonspecific phenomenon. It still remains to be shown if the various endogenic and exogenic stimulations are followed by and give rise to the same eliciting effect, for example, a change of the calcium content of the blood. Besides the histologic similarity, however, the otosclerotic osteosis is characterized by certain peculiarities or differential signs, in the first place the very peculiar localization and the extremely slow course of the bone process. As compared to other fibrous osteodystrophies, the otosclerotic process seems to take a very protracted course. This fact indicates that besides the known causative factors which give rise to bony dystrophies, one or more still unknown factors must be at work, which according to their character may induce a similar process with a different rate of speed.

The participation of the labyrinth capsule in a case of congenital osteogenesis imperfecta (female child of two days) was described by M. Weber (1930), who called attention to its significance in relation to similar processes in the onset of otosclerosis. The endostal capsule there consisted of a narrow layer of pathologically altered fibre bone. The enchondral capsule was essentially represented by a marrow space. Abundant cartilage remnants were found on which a malformed fiber bone was deposited, locally demonstrable as an intermediate stage between osteoid and chondroid. Lamellar bone

was entirely missing and osteoclasts were likewise absent. The periosteal capsule consisted throughout of a framework of pathologically altered fiber bone, denser towards the enchondral capsule. The bony changes of the labyrinth capsule had the common characteristic of a generalized fetal arrest and faulty differentiation of the bone forming system, with a relative left-sided displacement of the bone picture. The labyrinth capsule in this case fundamentally showed the same changes as the remaining bones of the skeleton.

The genesis of the otosclerotic focal lesion consists in all probability in a degenerative change of the old labyrinth bone, as pointed out by Lange (1929), who on the basis of new material proceeded to investigate the first beginnings of the otosclerotic process. His material consisted of forty-five histologically examined cases of otosclerosis; in twenty-one cases both sides could be examined, and both were affected in twenty of these cases. Twenty-six patients were men; fourteen were women; of five cases the sex is unknown. These figures are emphasized because otosclerosis is still believed to occur more frequently in women than in men. The seat of the foci was predominantly at the windows; they were remarkably symmetrical in the cochleas. The foci in the labyrinth capsule proved especially suitable for the study of the first beginnings, the objective of this particular study. Lange believes that the opposing views expressed in the literature can be reconciled, up to a certain degree, in his mode of interpretation: The otosclerotic focal change is to be regarded, morphologically and genetically, as a uniform process, no matter where in the labyrinth capsule it has developed. It begins with a pre-stage, which represents a degenerative process in the bone and cartilage of the enchondral labyrinth capsule. The extent of this pre-stage is variable in range and depends on the time of onset of the cartilage stage, although the pre-stage may still continue to grow. The degeneration is by no means a simple tissue necrosis, however, but the process starts directly with a structural change, being an active and not a passive process. The pre-stage is followed by the cartilage stage; onset beginning with the renewal of vascular supply. New active processes now set in and cells with dark nuclei are seen again in tissues previously devoid of nuclei. The origin of these cells, from cartilage remnants or from the vessels, is still debatable. The cartilage stage is primarily the stage of change and growth of the otosclerotic process. Through lacunar absorption active decomposition occurs, not only within the focus, but also within the unchanged labyrinth bone which is broken down beyond the boundaries of the pre-stage, and the gaps filled with cartilage and bone-forming tissue.

Hyperostotic thickenings of the capsule originate only in the presence of very active transformation and apposition processes during the cartilage stage. Apposition and growth of the cartilage stage are especially pronounced at the windows, where no decomposition of bone is required for the growth of the focus; exostosis-like thickenings are common in this region. The bone stage represents the ultimate ossification of the focus. It takes place through osteoblastic ossification and also through direct cartilage ossification. As a rule, it leads to a compact bone focus of irregular lamellar structure. The bone stage, however, does not always lead to the formation of compact bone. Pre-stage, cartilage stage and bone stage are often encountered in the same focus.

On the basis of various considerations, Doederlein (1928-1933) is inclined to assume that the process of change in the bone is similar to that in rickets or osteomalacia, so that a general cause is presumably responsible in all these affections. Certain differences of the bone changes in otosclerosis are readily accounted for by the peculiar structure of the labyrinth bone as compared to all other bones of the body. Clinical experience in otosclerosis would seem to bear out this assumption.

Demineralization of the bones is charged as the causative factor in otosclerosis ("otospongiosis") by Paliard (1930), who considers the ear disease as of essentially the same nature as other osteodystrophies, while restricted to the bony capsule of the labyrinth. Not an actual deficiency of phosphorus and calcium is responsible, but rather a deficient fixation of these two elements, which are excreted without having been properly utilized by the tissues. Functional disturbances of the endocrinic glandular system are the recognized cause of such demineralization processes and he assumes that the thyroid is probably primarily active in this regard through hyperfunction in otosclerosis.

The new bone formation in otosclerosis, according to O. Mayer (1928-1932), is a resorptive new formation of a primitive reticular bone; this process takes place at certain definite sites in the labyrinth capsule, namely, at the windows, and occurs in the form of foci or bands, which surround these sites in the form of rings. Because of its peculiar situation and its tendency to hyperplasia, the new bone formation has been described as a tumor-like hyperplasia. Mechanical strains are held responsible for this new bone formation. The osteogenesis of otosclerosis is of callus type and is referred by Mayer and others to a mechanical-functional origin. Its objective is to build

resistant bone at the points exposed to the greatest strain. In his monograph on otosclerosis (1917) the focal affection was interpreted by Mayer as a special form of tumor-like hyperplasia and was grouped under the heading of the so-called hamartomas.

The early stages of otosclerosis are described by S. R. Guild (1930) on the basis of his findings in eight cases—all from Johns Hopkins Hospital—in which otosclerotic foci were revealed microscopically after death. From the clinical viewpoint, these were early cases, although histologically some of the foci were evidently not of recent formation. The patients were two females, seventeen and thirty-eight years of age, respectively, and six males, ranging in age from one year ten days to sixty-eight years of age. The observer's study of the sections taught that otosclerosis may begin as early as the first year of postnatal life, a much earlier age than hitherto demonstrated. In his illustrative case in the infant, both temporal bones showed an abnormal osseous structure, similar to that seen in the early stage of otosclerosis, near the oval window on both sides. No similar changes were found in more than twenty other series of sections from infants of about the same age. On both sides the otosclerotic tissue was not in a single mass, but scattered in small areas along the anterior and most of the superior margin of the oval window. A narrow area of sharply demarcated otosclerotic bone with relatively large marrow spaces was also found on both sides at the promontorial margin of the round window. The fissura ante fenestram was involved in this case and three others of the series of eight. The exact location of the primary change was not always the same in this material. Before stapes ankylosis occurs a sulcus is frequently present in the otosclerotic area near the margin of the oval window; this sulcus is filled with dense fibrous tissue that extends across and fills in the space between the wall of the fossa of the oval window and the medial end of the anterior crus of the stapes. In some cases at least, stapes ankylosis begins by the formation, growth and coalescence of scattered areas of calcification in the fibrous tissue as well as in the annular ligament. An area of otosclerosis may arise near the anterior margin of the oval window, grow to considerable size and become quiescent without formation of any calcified connection with the footplate of the stapes.

Greifenstein (1935) raised the important question whether the histologic picture of otosclerosis occurs solely and exclusively in the labyrinth capsule, or whether the same or a similar picture is to be found under certain pathologic conditions also outside of the labyrinth capsule? Should this be the case and should moreover the rea-

sons be known for the origin of such otosclerotic pictures outside of the labyrinth capsule, valuable indications would thereby undoubtedly be furnished for the origin of otosclerosis itself. This question was approached by Greifenstein, of the Munich Clinic for Throat, Nose and Ear Diseases, on the basis of extensive studies of the bone tissue by means of polarized light. In his opinion, an otosclerotic focus, judging from its biologic behavior, may originate anywhere in the presence of vascular marrow spaces with specific germinal tissue.

Is there a "pathology" of otosclerosis? (Exuberant callus). In consideration especially of O. Mayer's theory of a mechanical-functional genesis of otosclerosis and Greifenstein's recent histologic studies, the question arises if the labyrinthine bone formation and deafness-producing bony obstruction of the oval window, is not to be interpreted as a physiologic protective defense mechanism that overshoots the mark, rather than as a "pathological," i. e., diseased process? Greifenstein's comparative investigations on the histology of otosclerosis (1935) led to the result that the focal affection of the labyrinth capsule does not represent a specific osseous change, but that fundamentally identical microscopic findings can be shown in bone regeneration and in structural alterations of the most variegated kind which histologically take their course under the picture of osteodystrophia fibrosa. The study of specimens and fibrils with modern tinctorial and optic methods repeatedly provided new data as to their finer histologic structure. Taken as a whole, these comparative investigations permit the conclusion that the young otosclerosis focus constitutes a regenerative new formation after a preceding osteoclastic resorption of the labyrinth capsule, namely, a so-called resorptive newformation. This comparative-histologic argument is further strengthened by an important biologic evidence to the effect that after traumatic injuries the marrow tissue of the young otosclerosis focus exhibits a lively regenerative activity in the sense of normal callus formation. Greifenstein's work aimed essentially at the elucidation of two main inquiries: (1) Are there any changes to be found in bone pathology in general ranking with some or other manifestation of the otosclerotic process? (2) Is the so-called "blue otosclerosis bone" to be interpreted as a degenerative product of the labyrinth capsule or as newformed young bone substance? The second question necessitated a comparative study of bone regeneration, more particularly callus formation, and the pursuit of its histologic course in shaft bones as well as also in the petrous bone and labyrinth capsule. Regenerative processes, derived from an otosclerotic process

itself, permitted significant conclusions as to the nature of the focal disease. The structure of the bone was regularly examined in polarized light. The typical histologic changes of the disease are discussed by the author in an illustrative case with extensive otosclerotic change of the labyrinth capsule, presenting side by side all the essential forms and stages of the process. The cochlear capsule on the left side contained otosclerotic focal segments of all ages; the region of the semicircular canals showed characteristically arranged blue mantles, which locally formed larger compact foci. The observer endorses the view that the otosclerosis focus originates from the bone of the labyrinth capsule through osseous newformation after a preceding resorption, and not through any degenerative processes. Histologically an active progressive process was here at work. The destruction of the old labyrinth capsule starts exclusively through osteoclasts in small resoption marrow spaces, on a broad advancing marrow front or in far protruding "finger-shaped" marrow spaces. Osteoclastic processes, demonstrable at the blue mantles, had extended to these secondarily, being derived from a typical circumscribed young otosclerosis focus. Greifenstein points out that the intensively blue-stained young otosclerotic bone represents a primitive newformed plexus-like bone, whose scanty fibrils can be demonstrated primarily through examination in chromatic polarized light. Besides the extensive and fundamental histogenetic conformity in the two processes of bone regeneration and otosclerosis, the most important and startling result of this comparative study of bone regeneration (ordinary fracture callus, trephine defects, callus formation and regeneration of the bony labyrinth capsule in large defects) and otosclerosis consists in the fact that the young otosclerosis focus itself, or more accurately speaking, its marrow constituent, must be credited with very considerable bone-forming capacities. The regenerative capacity of the otosclerosis focus, like that of any osseous tissue, is dependent upon the amount and functional state of the existing specific germinal tissue. Close histologic and histogenetic relations exist between bony regeneration and development of the young otosclerosis focus.

Greifenstein was enabled to show that a primitive plexus-like bone tissue, poor in fibrils, rich in cement substance—which shows the typical blue stain of the young otosclerosis bone—is found occasionally also under normal conditions as fracture callus. It is noteworthy that this is found in localities where the regeneration takes a slow clinical course, conveying the impression of its being prevented from reaching its termination for some reason or other. Aside from

the microscopic structure of the otosclerosis focus itself, also the histologic conformity of young regenerated bone with the so-called blue otosclerosis bone favors the interpretation of the focus as a regenerative bony newformation after a preceding resorption. The regenerative capacity of the individual layers of the labyrinth capsule is dependent upon the presence of specific germinal tissue in the vascular marrow spaces. It is usually entirely missing in the enchondral capsule, which contains only small and obliterated vascular channels, rarely marrow spaces. The periosteal labyrinth capsule may participate to a variable degree in the callus formation, in conformity with its more or less compact structure. The main source of callus formation is represented by the opened perilabyrinthine spongiosa marrow spaces, by way of which an apposition of germinal tissue and callus on the actual labyrinth capsule may also occur secondarily. Through the demonstration of active normal callus formation after traumatism of the young otosclerosis focus, a biologic reaction of the same has now been demonstrated for the first time, furnishing proof to the effect that the marrow tissue of the focus possesses a high osteogenic potency, itself constituting a specific germinal tissue. The regenerative capacity of the otosclerosis focus is confirmed by the fact that neighboring osteogenic layers, on account of the slight regenerative capacity of the labyrinth, do not enter into consideration as an eventual starting point of the callus formation. Judging from its histologic structure and its biologic behavior, the otosclerotic focus may originate wherever vascular marrow spaces with specific germinal tissue exist. The similarity of bone cicatrix tissue and otosclerotic tissue has also been confirmed by the observations and experimental findings of van Gilse in Holland (1934).

An article by J. Gordon Wilson and B. J. Anson, published in 1933, brings a description of an area of otosclerosis found in the labyrinth capsule of a man. Models of the specimen from the Department of Otolaryngology of Northwestern University were prepared by the Born wax plate method. Photographs of the model and photomicrograph plates were exhibited. The discussion deals especially with the form and structure of the otosclerotic nodule as well as its relation to the surrounding portions. There were two relatively small foci between the main otosclerotic nodule and the cochlea; the main focus was limited to the site of predilection in the labyrinth capsule at the anterior margin of the oval window. It consisted of an anterior portion with lesser root-like extensions which reached partly around the superior and inferior margins of the oval window. The estimated length of the sclerotic area was 3.46 mm. When

studied as a separated enucleated mass, the surface toward the middle ear was found to be smooth; it formed part of the tympanic wall in front of the oval window. Much of the deeper aspect toward the internal ear was irregularly lobulated, the lobulations producing corresponding excavations in the normal bone. The root-like extensions formed the boundary of the oval window in its anterior half, but did not involve the stapedial ligament or the stapes. The basal part of the mass was exposed to both the tympanic and the vestibular surfaces except at its anterior limit, where it was exposed only on the tympanic side. In sections the diseased bone of this focus stained deeply red with eosin and was thus easily distinguished from the surrounding normal bone with the naked eye. The focus was traversed especially at its core by a network of anastomosing spaces, each of which contained a blood vessel with thin walls and a loose network of areolar tissue. This gave the diseased bone a spongified appearance. Generally the line along which the focus bordered normal bone was very distinct and wavy or crenated in outline. The central cavities in the sclerotic bone were larger than the Haversian canals in the normal bone but smaller than marrow spaces.

An illustrated contribution, entitled "The Fissula Ante Fenestram in an Adult Human Ear," by Barry J. Anson and J. Gordon Wilson, enriches the final number of the Anatomical Record, Volume 56, 1933. The authors point out that the existence has long been known, within the lateral wall of the osseous vestibule, of a minute fissure which extends from the tympanic cavity inward through the bone to a point just in front of the vestibular window. Models of this channel show that in the adult ear it begins as a crevice-like continuation of the vertical sulcus which on the labyrinthic wall of the tympanic cavity marks the posterior extent of the promontory. After traversing the bone in an inferior and posterior direction, the inner orifice of the fissula becomes continuous with the cavity of the internal ear just medial to the anterior extremity of the vestibular window, at a point where the vestibule becomes the scala vestibuli. In its course the long axis of the fissula changes through about 90°, being at first directed inward, then backward. Models representing the cleft-like space of the fissula show that its anterior and posterior margins are concave backward; also that its space communicates at several points with the Haversian canal system of the surrounding bone, through which communications the connective tissue of the fissula receives small blood vessels. Near the extremities the tissue enclosing the fissula is largely bone; otherwise, the fissula rests in modified cartilage (interglobular spaces). A further study of the fissula

is in progress; the structure is being modeled as it appears in serial sections of the ear from infants, children and older adults. (The specimen described in the foregoing was removed from the left temporal bone of an adult, eighteen years of age.)

In the experience of Hagens (1931) with regard to the fissula ante fenestram, the otosclerotic foci in his specimens were all too far advanced "for one to tell whether they had started from this structure or had engulfed it in their development."

The later examination of forty series of sections, from the collection of the Otolaryngological Department of the Northwestern Medical School, Chicago, by Anson and Martin (1935), showed that the fissula ante fenestram not only assumes different forms, but may also secondarily increase in extent, especially in youth, through communications with neighboring marrow spaces, or it may be reduced by an encroachment of new-formed cartilage or sclerotic bone. The latter not infrequently occurs in this area, partially or wholly obliterating the fissular connective tissue. In a specimen from an adult, eighteen years old, the fissular area was remarkable for the manner in which it terminates conventionally below, but widens above into a relatively large nodule, of sclerotic bone; between the two portions a cartilaginous strip intervenes. The fibrous tissue gives way to cartilage, the two tissues merging through a narrow band of perichondrium. The preponderant part of the entire mass is composed of a vascular spongious bone of the sclerotic type. The macroscopic nodule possesses the several features commonly regarded as characteristic of otosclerosis: It stains deeply with eosin, it contains large, thin walled blood vessels in capacious ramifying channels, which give to it a spongy appearance; the channels are enclosed by definitely lamellar bone. Sometimes the vestibular orifice is crossed by bridges of bone, suggesting that once it is established in the embryonic temporal bone both its shape and its size may be altered by the subsequent growth of osseous tissue. Normal bone is not the only tissue that remains productive in the fissular area, since with surprising frequency in young subjects immature cartilage is found in what undoubtedly was fissular space. Occasionally sclerotic bone in rapid development obliterates part or all of the fissular space. "The frequent occurrence of otosclerosis within the fissular territory leads one to suspect that a definite histologic succession occurs in this histologically mobile area."

The fissula is not infrequently incomplete, lacking one or both orifices. Its extremities may vary in relation to dependable land-

marks. The tympanal orifice is invariably more cranially situated than the vestibular.

The special interest to the otologist, of the histology of the area between the foramen ovale and the cochlea, as the site of predilection for otosclerosis, is emphasized by Gordon Wilson in a recent instructive contribution (1935). This area, which contains the fissula ante fenestram—a well marked feature often even in the adult—presents a diverse histologic structure, containing areolar tissue, connective tissue, cartilage and bone. The fissular area is one of potential activity even in older individuals, as shown especially in those cases in which it becomes obliterated by the growth of sclerotic bone, also by the ability to spread into adjacent marrow spaces. The development in this fissular territory of cartilage in the young and of sclerotic bone in older persons may be directly associated with its proximity to the rather abundant blood supply which comes chiefly from the middle ear. The occasional local interruption, at any stage, of the normal development of primitive tissue, cartilage, primary bone and intrachondral bone, is tentatively referred to a state of disequilibrium by the author, who is at present inclined to attribute an important part to the vascular factor.

According to the theory of O. Mayer (1924), the otosclerosis foci must be interpreted as callus-like formations, such as have been described in the so-called transformation zones in other portions of the skeleton. The hyperplasias and also stapes ankylosis in this interpretation originate as a result of nature's tendency to repair beyond actual needs. The very recent histologic findings of Greifenstein (1931) in his comparative investigation of bone regeneration and otosclerosis, as well as the conclusions derived therefrom, constitute an essential support of O. Mayer's otosclerosis theory.

According to the findings of Lange (1929), there are three stages in the development of the otosclerotic focus: The preliminary stage (blue mantles stage of Manasse), the cartilage stage and the bony stage. No definite evidence of growth by bone resorption and new formation was found in the lesions of the preliminary stage, and in his opinion these processes belong rather to the cartilage stage.

Knowledge of the osteopathology of the labyrinth capsule has been advanced by the work of Nager (1931), who points out that the middle layer of the labyrinth capsule, namely, the enchondral layer, differs from all other parts of the human skeleton in the absence of any developmental change during life and in the imperfect development of its tissue, as shown by the presence of cartilage

remnants, interglobular spaces and the absence of the normal Haversian lamellar system. The diminished vitality of this layer exposes it to bone diseases of inflammatory or erosive character (Paget's disease) and to affections with a fetal or infantile histogenesis, such as chondrodystrophia and osteogenesis imperfecta: the latter being of special otologic interest as a typical bone disease. Otosclerosis likewise begins in the enchondral layer. Nager is inclined to assume the action of a chronic irritative process of an endogenous chemical nature, which acts especially on the enchondral layer of the labyrinth capsule.

"Fractures" in the Labyrinth Capsule.—Fractures or fissures in the labyrinth capsule, due to a variety of causes, were found by Mayer (1930) to be an important factor in the production of otosclerotic foci. In his opinion, the cause of these fractures must evidently be sought especially in the static relations of the labyrinth capsule. The common premature senile changes of the capsule induce obliteration of the vascular spaces and necrosis of the osteocytes, resulting in a marked fragility of the internal capsule with a great tendency to fracture, whereas the surrounding tissue, which contains elastic and spongy bone, is flexible and especially yielding in the presence of pronounced pneumatization. The labyrinth region undergoes the greatest strain in any movement of the labyrinth apex. The otosclerotic foci are interpreted by Mayer as transformation zones which develop at the sites of the spontaneous fractures in the form of an insidious callus formation, for the fracture sites are also subsequently exposed to mechanical irritation. A special vulnerability of the labyrinth capsule, due to its composition of brittle compact bone, is held responsible for the occurrence of these spontaneous fractures.

The foregoing views are not endorsed by Brühl (1930), according to whom the fissures in the solid petrous bone tissue may eventually be of postmortem origin, in other words, artifacts; otosclerosis, being a degenerative affection due to constitutional factors, cannot be explained through ordinary traumatic causes. For the explanation of the focal development of the bony alterations, especially in the vestibular niche, the mechanical relations in the petrous bone were first systematically utilized by him. A number of objections are also raised by Nager (1931) against Mayer's interpretation of these fissures and fractures.

Brunner's (1931) study of twenty-six petrous bones from his own collection (derived from persons between nine and seventy-one years of age), with reference to the frequency of the fissures or spon-

taneous fractures in the labyrinth capsule showed fissures in the promontory in only two petrous bones in the whole series. An oblique fissure extending from the facial nerve canal to the upper bony capsule was noted in three petrous bones. In the bony wall of the cochlea, fissures were found only in cases of Paget's disease, with involvement of the petrous bone. The great majority of his specimens, or twenty-four petrous bones, presented fissures in the region of the semicircular canals, chiefly affecting the median portion of the bony wall of the recessus ellipticus. As a rule, the fissures originated in the endosteum, involved the endosteal bone and penetrated to a varying extent into the lamellar bone of the enchondral capsule. In some instances they extended through all the layers of bone. Their course was usually irregular. In the region of the round window fissures were found in only eleven cases of this series and in four cases were undoubtedly artifacts. The fissure in one instance was surrounded by an otosclerotic focus. Connective tissue, partially calcified in some areas, filled the fissures. In a few instances the narrow fissures were possibly of traumatic origin (injuries of the head or other parts of the body). In Brunner's opinion, the wider fissures with connective tissue content are not due to traumatism. He refrains from an explanation of the true nature and origin of these fissures, but does not agree with Mayer in their interpretation as the starting point of otosclerotic foci. The fissures were found in both the presence and absence of otosclerosis, most frequently where otosclerotic foci are rarest, and were least seen at the oval window, the site of predilection of otosclerosis.

Mayer's explanation as to the cause of fissures or fractures in the labyrinth capsule is not accepted by Leiri (1929), who refers the production of these fissures essentially to: (1) The pulsation of the carotid artery against the labyrinth. (2) The movements of the stapes footplate in the oval window. (3) The tension of the membrane in the basal coil. In addition to these purely mechanical factors, also other forms of irritation act upon the labyrinth capsule.

In the temporal bone specimens of the Leipzig Clinic, fissures were often found in the labyrinth capsule, most frequently in the superior semicircular canal, next in the region of the posterior ampulla. (Eschweiler, 1933.) Fissures more or less filled with tissue in the walls of the semicircular canals were seen in thirty-three of eighty specimens derived from persons over fifty years of age. But even youthful individuals up to twenty years of age sometimes presented fissures, although not as frequently as in old age and otosclerosis. In the observer's opinion, the tissue content of the fissures as well as

their localization and the absence of any reaction indicate their correct interpretation as artifacts. Lange (1929) likewise always observed the fissures described by Mayer in his temporal bone specimens and, like Eschweiler, he interprets them as artifacts. The observations of Kelemen (1933), who in a study of adult temporal bones often found fissures in the labyrinth capsule, do not permit him to draw conclusions as to the relation of such fissures to otosclerosis. Also Loebell and Nack (1933), who carried out a study of the labyrinth capsule on twenty-seven specimens (twenty-one from adults, four from newborn infants, and two from embryos) do not discuss the significance of these fissures or their eventual relation to otosclerosis. The fissures were found in O. Mayer's six typical areas.

A number of writers, for example, Dundas Grant, in collaboration with Ormerod and Simmonds (1929), have reported cases of osteopsathyrosis, bony fragility, and so forth, with blue sclerotics, and have called attention to an eventual connection with otosclerosis. Four or five cases of abnormal bony fragility, blue sclerotics and hardness of hearing, reported by Friedberg (1931), were associated with deafness. From the study of his clinical material and a review of the literature, the observer concludes that the syndrome of bony fragility, blue sclerotics and deafness is not due to a defective development of either the mesenchyme or the mesoderm, but represents a combination of several genotypic anomalies. The deafness of this syndrome is due apparently to otosclerosis or to labyrinthine disease, both occurring in the same family or even in the same individual. Otosclerosis and degenerative labyrinthine deafness, according to the theory of Bauer and Stein (1924-1925), develop on the same genotype basis. From his study of three generations, the second and third of which presented the entire or partial syndrome of bony fragility, blue sclerotics and auditory disturbances, Tanturri (1931) concludes that in all cases of bony fragility a careful otologic examination is indicated also in the absence of typical symptoms of otosclerosis, as it may reveal latent lesions in the cochlear or vestibular apparatus. Atypically situated otosclerotic foci in the labyrinth capsule may be responsible for existing disturbances of the vestibular and cochlear function. The underlying cause of osteopsathyrosis, otosclerosis, and other dystrophic bone diseases is suggestive of endocrine functional disturbances, which together with biochemic factors exert an influence on the development of bone.

The changes in the labyrinth capsule in Paget's disease, with slowly progressive deafness, as pointed out by Beck (1933), on the

basis of a personal observation, are not necessarily of otosclerotic origin. All the capsular layers may be involved in the bone disease, with production of the same symptoms as by otosclerotic changes.

Attention is called by Lewis (1932) to the fact that between the fifth and tenth years of life the labyrinth capsule of certain individuals manifests the abnormal bone changes of "otosclerosis." These are in no way associated with health, they neither result from illness nor impair the health of the individual, directly or indirectly, as do toxic or infectious processes. Otosclerotic bone changes show reversions to immature and embryonal characteristics, among which is the devotion of cell activities almost exclusively to growth; in this respect otosclerosis might be described as "anachronistic" rather than pathologic. Clinical manifestations of otosclerosis are confined to evidences of mechanical effects of abnormal bone growth. In approximately similar locations, certain neoplastic bone changes (exostosis, hyperostosis, osteoma) are accompanied by certain other effects—local pressure, pain and soft tissue changes. Otosclerotic tissues do not tend to break down; these neoplastic tissues do; the otosclerotic process speeds up during the physiologic changes concerned with puberty and pregnancy; these neoplastic processes do not. The fact that otosclerotic cell activities are increased during puberty and pregnancy sheds some light on the nature of the abnormality. Some intracellular agency determines the direction of cell activities; at one stage, predominantly to growth; at another stage, to other activities; otosclerotic cells act as if in them this agency were in the state normally found during embryonic life, at which stage such cells are "growth-minded," particularly stimulable by something whose concentration in the body is ordinarily increased during puberty and pregnancy. Microscopic search through many specimens fails to reveal details of bone cell structure whereby one might attempt to differentiate "normal bone," "otosclerosis," "osteogenesis imperfecta," or "osteodystrophia fibrosa." Yet it seems not only possible but even probable that such structural differences do exist.

In his contribution entitled "The Bone Picture of Otosclerosis," Weber (1930) considers otosclerosis as the end-result of some complicated process which is not yet definitely known. It is regarded by him as a pseudotumor, resulting from maldifferentiation, which may originate from a faulty anlage, but which may also be caused by a secondary dystrophic disturbance very early in life. For the experimental production of otosclerosis in animals some species must be discovered and selected in which the labyrinth capsule is anatomically similar to the human organ. The presence of cartilaginous remnants

is essential and the induction of the dystrophy destined to change the bone picture to that of otosclerosis in the laboratory animal must begin very early in life, if not prior to birth, through disturbance of the maternal endocrine balance. An irritation of the bone-forming system must be produced that attacks the areas of predilection leading to a local progression; and at the same time the advance must be arrested and a tendency to faulty differentiation produced. Otosclerosis not infrequently is found associated with generalized osteodystrophia fibrosa or osteogenesis imperfecta; and the experimental reproduction of otosclerosis may be attempted on the basis of one or both of these diseases. In association with his collaborators, Weber (1930) found that typical osteodystrophia fibrosa can be produced in dogs by feeding a restricted diet poor in calcium and entirely lacking in vitamin D. The experimental bone changes corresponded to those in a dog in which the disease occurred spontaneously. But neither in this spontaneous case nor in the experimental cases in dogs was true otosclerosis produced in the labyrinth capsule, which presented a hypo-ostotic form of osteodystrophia fibrosa. The failure to produce otosclerosis in these animals, in Weber's opinion, was due to the fact that the cartilaginous remnants had disappeared from the labyrinth capsule when the feeding experiments were begun. Where such cartilage remnants were present in the long bones, the bone picture of osteodystrophia fibrosa was especially well marked. Had such remnants been present in the labyrinth capsule, they would have been the first to be attacked by the dystrophic process, with resulting degeneration and resorption. The products of disintegration would have led to the local increase of irritation primarily started by the dystrophy, giving rise to a pseudotumor (hamartoplasia), or true otosclerosis. The latter might thus be produced experimentally, on the basis of osteogenesis imperfecta, by creating a special irritation in the labyrinth capsule. Venous stasis, according to Wittmaack's method, appears to be well adapted for this purpose. Weber doubts the possibility of producing the hyperplastic form of otosclerosis without some general disturbance of the metabolism. Biochemical analyses have shown that otosclerosis is always accompanied by some metabolic disturbance that might influence the bone system; this metabolic disturbance is not necessarily the same in all cases of otosclerosis. Possibly all the metabolic disturbances noted in otosclerosis have a common factor, as yet unknown. Meanwhile different etiologic factors may produce the same end picture. Thus the bone picture of otosclerosis theoretically may be produced experimentally in various ways. But if the typical bone picture of otosclerosis is successfully produced in animals by any method, it will be possible to ascertain the etiologic

factor or factors that are responsible for its spontaneous appearance in man.

Goldinberg (1929) describes peculiar changes of the bone of the internal ear capsule, at the base of the cochlea and the internal auditory meatus, in a congenitally deafmute woman, thirty-one years of age. The osseous ground substance showed a remarkably fibrillar and extraordinarily loose structure. The bone fibers took in part a parallel, in part a plexus-like course. At the wall of the tympanic cavity and in the environment of the stapes, pathologic bone foci of the type of otosclerotic bone were found, also cartilage islands. These bone changes are considered by the observer as part of the otosclerotic picture.

In his "Bone Picture of Otosclerosis," five "time phases" were distinguished by Weber (1930), in normal bone development: (1) The fundamental stage, namely, the mesenchymal tissue. (2) The stage of increase and differentiation of intercellular substance and differentiation of cells surrounded by the latter. (3) The stage of "nucleus" formation, namely, the stage of hardening of the various differentiated intercellular substances by lime impregnation. (4) The stage of shell bone formation formed by osteoblasts in epithelioid formation, representing the highest unit of bone formation. (5) The stage of resorption, either directly by means of vessels or by osteoclasts. "Pathologic changes in bone find their expression in alterations of the time phases of the normal bone picture." Weber repeats previous statements to the effect that the bone picture in otosclerosis is identical with the findings in localized osteodystrophia fibrosa. The bone changes in otosclerosis are analyzed by him as follows: (1) The time element: It is difficult to determine when the disease begins; it may begin in utero, but it is certain that the bone formation in otosclerosis is completed during the postfetal period. (2) The space element: Otosclerosis is confined to definite areas in the labyrinth capsule, these areas being closely related to cartilaginous remnants and to cartilage and connective tissue portions, namely, the fissura ante fenestram or Cozzolino's zone. (3) The element of quantity: The bone picture shows: "A displacement to the left," in analogy to the blood picture, that is, the earlier stages of differentiation are increased in quantity, indicating an irritation of the fundamental stage (stage 1) of bone formation and a consequent progression. The highest unit of bone formation (stage 4: bone formed by osteoblasts in epithelioid formation) is absent. This may be interpreted as a sign of regression or an arrest in development. If the total amount of apposition exceeds the limit of normal apposition, as in

the hyperplastic form of otosclerosis, there is an "absolute" displacement to the left; if the total amount of apposition does not exceed the normal limit, a "relative" displacement to the left. (4) The element of quality: Otosclerosis shows a malformation as a result of faulty differentiation of the bone forming system. This finds expression in qualitative changes of all the time phases of the bone picture; in the formation of fibroma-like areas and pathologic fiber bone that stains blue with hematoxylin; also occasionally in cyst formation; and in the development of other varying bone pictures. A fifth factor of bone formation, namely, speed of the process, added by Bast (1927), is credited with great importance in the determination of the finished product as web bone or lamellar bone, with their intermediate stages. The difference is one of degree, not of type. In his opinion, all localized otosclerotic patches are of one type, but differ in degree owing to different speed of development. As speed is a function of time and space, it was included by Weber in his definition of the bone picture.

The investigations of Hirschmann (1934) on the "blue sclerotics group" are based on six illustrative cases in four families. The observer was enabled to show, aside from the three classical symptoms, blue sclerotics, bony fragility and otosclerosis, also changes of the shaft bones, changes of the bony skull capsule, protuberances of the occipital bone, enlargement of the posterior cranial fossa, protuberance of both temporal scales. In addition, a premature ossification of the cranial sutures could be demonstrated. Furthermore, relaxation of the ligamentous apparatus was shown, as well as deficient solidity of the joints, notably the ankle joint. Three cases presented a lymphatic constitution. Relative lymphocytosis and increase of the blood platelets were other noteworthy features. A genealogy of five generations showed a dominant heredity with transmission of blue sclerotics only in the male members of the affected families. At the annual meeting of German Oto-Rhino-Laryngologists in the Czechoslovakian Republic, held in Prague in November of 1933, Kohn described two typical cases of osteopsathyrosis in father and son, both with blue sclerotics and incipient otosclerosis. Special interest in these cases was attached to the behavior of the pneumatization in the domain of the petrous bone. In the first place, there was an extraordinary extension of the pneumatization in the mastoid process, filling the entire petrous bone with pneumatic cells. The labyrinth appeared relatively reduced in size through this extraordinary extent of the pneumatic system, which naturally weakened the resistance of the bone.

The roentgenologic examination of the temporal bones of patients with otosclerosis led Dillon and Preobraschensky (1930) of the State University of Moscow to the conclusion that in these cases the pneumatization of the temporal bone may be equally variable as in other persons. The structure of the temporal bone was found to exert no essential influence on the course of the otosclerotic process. As a rule, the process is restricted to a very small area of the labyrinth capsule and also further on exerts no notable influence upon the osseous structure. This behavior may be explained by the fact that the evolution of the pneumatization process of the temporal bone, at least in its main portion, is already completed before the otosclerotic process sets in and manifests itself. No definite relation could be established between the degree of the auditory disturbances and the degree of pneumatization of the temporal bone in patients afflicted with otosclerosis.

Hagens, in 1930, described in detail the pathologic findings in four temporal bones from three cases of otosclerosis; in only one of these cases had the diagnosis been definitely rendered during life. Five additional cases were reported by him in 1931. The prominent staining of the foci with hematoxylin-eosin is possibly due, in his opinion, either to the unusual attraction of the focus bone for the mordant in the stain or to the presence of iron. A number of observers have thought the peculiar staining was due to the excess of calcium in the focus, but this could not be proved. Five years after his first report, Hagens (1935) still finds no adequate theory of etiology and no wholly satisfactory descriptive term for the pathologic process.

In a study of adult temporal bones, fissures were often found in the labyrinth capsule by Kelemen (1933), but could not be brought into correlation with otosclerosis in his material. However, he is inclined to agree with O. Mayer that such fissures may be due to functional strain. According to cautious observers, some of the fissures, but not others, induce the otosclerotic reaction in the form of focus formation.

The blue mantles in otosclerosis were discussed at the Second International Oto-Rhino-Laryngological Congress (Madrid, 1932) by M. Weber, who has examined fifty-one human temporal bones of otosclerosis, showing no signs of Paget's disease. In all the fifty-one labyrinth capsules the bone surrounding the otosclerotic focus showed processes of transformation. This osseous change appeared in the form of perivascular, so-called blue mantles (Manasse, 1922),

in 28 per cent of the examined ears. The blue mantles were shown to consist of a primitive, mainly plexus-like pathologic bone tissue newly formed from the vascular spaces after preliminary lacunar absorption of the surrounding bone. The remaining 72 per cent showed red mantles and mixed mantles. The mixed mantles consisted partially of plexus-like bone and partially of lamellar bone. The red mantles consisted only of lamellar bone. All these perivascular areas followed preliminary absorption. The investigation of fifty-one human labyrinth capsules of otosclerosis led to the following conclusion: Otosclerosis cannot be regarded generally as a pure primary focal disease, but must be regarded as a disease at least of the whole labyrinth capsule. Further research will have to clear the question whether in every case of otosclerosis the general bony system shows pathologic changes or not. In a later publication (1933) the author again arrives at the conclusion that otosclerosis appears actually in the form of a focal disease, but the labyrinth capsule around the focus showed transformation processes in all his examined cases. Therefore otosclerosis should not be regarded generally as a primary focal disease of the labyrinth capsule. One should consider it rather from the standpoint of histopathology and take in account the fact that the labyrinth capsule surrounding the focal disease shows pathologic changes, as a rule.

Deafness due to rickets is considered as extremely rare, but Yearsley (1933) reported a case of complete deafness due to rickets in a girl of four years, who had been deaf since the age of twelve months. The demonstration of the "salmon reflex," usually associated with otosclerosis, suggests that changes similar to those in other bones existed in this child's labyrinth capsule. Impairment of hearing was observed by Schneider (1933) in three cases of osteopsathyrosis or bony fragility with blue sclerotics, two of these with multiple fractures. In all these cases a diagnosis of otosclerotic deafness was rendered.

In the discussion of Fowler's paper on "Otosclerosis Complicated by Other Lesions," presented at the sixty-sixth annual meeting of the American Otological Society, Washington, in May of 1933, Guild referred to otosclerosis as an osteitis in its essential features, whatever its etiology may be.

In a later paper Weber says otosclerosis is based on a premature transformation of the labyrinth capsule, which otherwise does not occur until an advanced age. This inferiority is dependent upon the mesenchyme, which is the carrier of

the hereditary substance. The histologic picture resembles that of osteodystrophia fibrosa. In 10 per cent of the histologically examined petrous bones otosclerotic foci were found, the youngest cases concerning the sixth year of life. Only 25 per cent of all histologically demonstrated otosclerotic foci presented a stapes ankylosis. Weber outlines the classical picture of otosclerosis and enumerates the many deviations which often interfere with a certain and early diagnosis.

At the fifty-fifth meeting of Dutch otolaryngologists, Amsterdam, May, 1933, Gilse (1934) demonstrated specimens showing bone decomposition and transformation in the petrous bone. Differences in pressure and tension presumably cooperate in this process.

V. CIRCULATORY AND INFLAMMATORY FACTORS. VENOUS STASIS.

Wittmaack's (1930) venous stasis theory on the genesis of otosclerosis is based upon the explanation of the local absorption process as a bone absorption which is elicited through a venous stasis with considerable rise of the venous blood pressure. Under normal conditions, the venous blood stream evidently takes a slightly ascending course from the site of emergence of the auditory vein, traversing the tympanic roof from below upward, predominantly, although not exclusively, accompanying the major superficial petrosal nerve, and together with this nerve emerges from the cranial cavity. Under the pathologic conditions on which the evolution of the otosclerotic process is based, however, the blood stream within the venous tracts here concerned evidently follows the opposite direction and is forced in a retrograde course into the emerging vein of the area of special predilection. In addition, there is probably also a certain reversal of the venous blood stream within the veins of the mucosa in the domain of the promontory. This behavior evidently accounts for the peculiar change and reddish shimmer of the promontory (promontorial blush) in the otoscopic picture. This reversal of the venous blood stream within the drainage area here concerned is referred by Wittmaack (1930, 1931) to the onset of a certain insufficiency of drainage within the carotid plexus or the venous plexus of the middle meningeal artery. He emphasizes that the otosclerosis problem can never be entirely understood, let alone solved, by looking exclusively at the otosclerotic absorption process itself. It is only by way of the peculiarities of the focus and a careful study of its vicinity, with special attention to the venous drainage paths, that the connection will be clearly shown between the otosclerotic focus and the characteristic reversal of the blood current within the venous tracts, which are to be regarded as the actual cause of the diseased focus. The retrograde venous blood stream, which is forced into the bone veins under considerable pressure, must necessarily induce, on the one hand, acidosis of the surrounding tissue fluids with solution of the calcium salts in the domain of the dilated vessels; while on the other, the intensive flow and fluid infiltration within the affected tissues must also be followed by a radical change in the position and in the behavior of the bone fibers. The pathologico-anatomic changes in the bone are due, according to Wittmaack (1932), to transformation of the old bone, but not to bony new mation, as can be positively shown by animal experimentation.

The following arguments in favor of Wittmaack's theory of venous stasis as causing otosclerosis are advanced by C. F. Werner (1931) of Wittmaack's laboratory: In the human labyrinth bone, the distribution of blood vessels is determined by ossification centers and is of such a nature as to contribute to the onset of stasis, because it is not relieved by anastomoses with neighboring vessels. Although the labyrinth capsule of the hen differs in certain particulars from the human capsule, it represents essentially the same type of structure. It likewise develops on cartilage; it has three layers; the middle enchondral layer is lined with a thin bony endosteal layer and covered with a thicker outer bony layer; as in man, embryonic cartilage remnants may persist throughout life. In the hen, the ossification of the labyrinth capsule is complete at the latest by the ninth month of life. The hens used by Wittmaack in his experiments were at least two years old, so that the changes demonstrated in the labyrinth capsule in these experiments cannot be attributed to any developmental anomalies; they are not present in normal hens of the same age. There is a difference in the vascular system of the labyrinth capsule in man and in the hen. In man, the vascular distribution determined by the centers of ossification persists throughout life. Consequently, venous stasis would have a strictly localized effect, with production of local lesions, more particularly at the oval window, the site of predilection for otosclerosis. Because the periosteal capsule is thick and compact, the regional veins pass separately for a considerable distance through this bony wall before reaching larger venous spaces. This circumstance favors the occurrence of venous stasis, which would be strictly localized, should it eventuate. The hen is provided with a large venous sinus accompanying the semicircular canals; if such a stasis is produced in this sinus (as in Wittmaack's experiments) the stasis then affects the labyrinth capsule diffusely. The difference in the venous distribution explains the difference between the localized focal lesions of otosclerosis in man and the bony changes of the entire labyrinth in Wittmaack's hens. The essential nature of the process is identical.

Wittmaack himself raises the pertinent question as to the cause back of the venous stasis. There may well be a multiplicity of causes bringing about this condition. The venous stasis theory does not conflict with the established hereditary predisposition to otosclerosis in a certain percentage of cases. A special inherited proclivity to premature dysfunction of the vascular walls may possibly be a powerful factor in the production of venous stasis. The principal vein from the common otosclerotic focus in the vicinity of the oval window,

the source of the clinical disease, is imbedded in rigid walled surroundings and does not directly join one of the branches of the jugular vein, but passes into the pterygoid plexus. Venous stasis in this region would presumably be favored by the noted anatomic peculiarities. Human otosclerosis is accordingly referred by Wittmaack to a stasis of blood within the veins of the bone. Unsuccessful attempts were made by him to produce otosclerosis through venous stasis in a large number of monkeys (sixty to seventy), leading him to infer the existence of some additional factor in the production of the disease. In view of his demonstration of such marked venous congestion in the majority of his otosclerotic cases, he suggests (1933) that a backflow of blood into the focus may be present, and may possibly be arrested by surgical division of the regional veins draining the otosclerotic area.

The objections raised by Wittmaack against the otosclerosis theories of O. Mayer, from the vascular theory of 1911 through the hamartoma theory of 1917 to the spontaneous fracture theory of 1931, should be consulted in the original. Nothing like otosclerosis is ever seen in any other part of the skeleton, because the blood supply of the capsule is entirely different from that of the enchondral bone elsewhere in the human body. The study of the disease must necessarily be based on the anatomy of the capsule in laboratory animals, as was done by Wittmaack under employment of his new experimental technic in the early stage, by means of blocking the venous return and creating a venous back flow through the bone. The contention that Wittmaack's experiments on hens are untenable on account of the alleged absence of typical cartilage remnants in the hen's labyrinth capsule, has been refuted by Wittmaack's disciple, Werner (1931). The objection that the change produced in the hen is not similar to human otosclerosis because it is not focal, is answered by the fact that the experimental otosclerosis occasionally does occur in foci; and furthermore, because otosclerosis is occasionally so widespread that it can hardly be defined as a single focus disease. Wittmaack's investigation of O. Mayer's "spontaneous fractures" has led him to entirely different conclusions (1933) as to their origin; he not only denies the existence of true fractures—many are undoubtedly artifacts—but he emphasizes that even granting the existence of genuine fractures, no light would thereby be shed on the otosclerosis problem, because the debatable changes do not occur at the points of predilection for otosclerosis.

A probable vascular nature of the disturbance of chronic progressive deafness, including otosclerosis, was pointed out, on the basis

of personal observations, by Josephson, in 1929, as confirmed by the response of these cases to vasodilators and constrictors, referred to in the preceding year by Albert Gray. The gross vascular changes described by Josephson in the external auditory canal resemble the vascular changes demonstrated in the pathology of chronic progressive deafness. In conjunction with the response of the auditory apparatus to vasodilator and vasoconstrictor drugs, these changes are interpreted by him as indicating that the essential feature of the pathology of chronic progressive deafness is a disturbance in vascularity associated with changes in the vascular bed in the petrous bone. The hereditary nature in many cases is explained on the basis of a congenitally narrow vascular bed in the labyrinth and a nonanastomotic distribution of the labyrinthine artery.

Circulatory disturbances in the terminal branches of the nutrient bone arteries of the petrous bone have long been charged as responsible for the focal osseous disease in otosclerosis. The existence of symptoms referable to vasomotor disturbances in some otosclerotic patients was mentioned by Mayer (1911). In the early stages of otosclerosis, signs of congestion in the form of considerable vascular dilatation, apparently due to obstruction of the normal venous outflow, were noted by Heyninx (1924). These findings, as well as the observations of Grünberg (1926-1927), may be interpreted as confirmatory of Wittmaack's theory of venous stasis.

In a rare case concerning a man, forty-one years of age, Charschak (1934) observed a circulatory disturbance in the form of embolism of the internal auditory artery, followed by damage of the petrous bone. As a sequel of a furuncle on the chin, with subsequent osteomyelitis of the left arm, all functions of the right labyrinth were suddenly suppressed, presumably due to labyrinthine disease of vasomotor character. An embolus from the osteomyelitic focus had to be assumed as the cause of this disturbance. When the embolus reached the terminal vessel, namely, the internal auditory artery, blocking the cochlear and vestibular branch and thereby interfering with the nutrition of the labyrinth, the picture of sudden deafness and vertigo supervened. The condition was finally interpreted as circumscribed meningitis and damage of the petrous bone. Operative intervention revealed complete destruction of the labyrinth and a deep seated lesion of the petrous bone. Removal of the damaged portion and provision of wide drainage were followed by further conservative treatment, which the observer credits for the favorable outcome. The gradual compensation of one labyrinth by the other is an interesting feature of this unusual case.

A factor of great importance in the individual predisposed to otosclerosis is sought by E. P. Fowler (1933) in the inflammatory episode, which in his experience seems to be so common in all individuals, although often ignored or unrecognized. His data were collected for over six years, and 126 cases diagnosed as otosclerosis were analyzed with the aid of the latest laboratory and instrumental adjuvants. In no instance was there lack of evidence of inflammation in the microscopic sections, of forty cases of definite otosclerosis. Inflammatory processes, as emphasized by Fowler in his conclusions, are not to be ignored as factors in the deafness accompanying otosclerosis and in its etiology. In these cases of otosclerosis there is a much higher percentage of sinus pathology as compared to the twenty controls and a different variety of type of sinus pathology than encountered in cases of sinusitis not coincidental with otosclerosis.

The statement of Guggenheim, in the discussion of the foregoing arguments, to the effect that he had never seen evidence of an inflammatory process in otosclerotic areas, was countered by Guild with the remark that in the so-called "active" stage the process frequently has a histologic appearance which so resembles some features of osteitis that it seems to him entirely possible that fibrous tissue may be produced by the reaction.

A paper in support of the hypothesis that inflammatory diseases precede otosclerosis, and that the evidence tends to show that it is a local rather than a general disease, was read by E. P. Fowler, Jr., at the sixty-seventh annual meeting of the American Otological Society, in Atlantic City, April, 1934. His findings, in his opinion, support the evidence previously presented by Fowler, Sr., that signs of inflammatory disease in the past may be seen in all cases of otosclerosis. Based upon continued studies along this line of inquiry, Fowler, Jr., has reached the conclusion that otosclerosis is a reaction to a local process, possibly a thrombosis of vessels, in the promontory or elsewhere, in the course of a known or "masked" otitis media. Some resorption and regrowth of bone is to be seen in other parts of the labyrinth capsule than the sites of predilection. This indicates, as one might expect, that interference with the blood supply to the bone in other areas, also produces resorption and regrowth of bone. It is only the unprotected location of the anterior part of the niche for the stapes, the probability that its blood supply would most easily be affected, its bizarre normal structure and the fact that it may cause symptoms, which make otosclerosis stand out so prominently here. Also there is a strong probability that predisposed individuals might have vessels in this region which were more open to attack or have

anastomoses insufficient to provide for the emergency of thrombosis of the vessels over the promontory. In ultra violet light, the fiber structure of otosclerotic foci shows it to be new bone, often as primitive in type as the bone of the normal enchondral capsule. Later the primitive bone may be partially replaced by a lamellar or "shell" type of bone, but this is not the initial process. The important point is that the first bone formed is similar to that of a healing process in any other bone of the body which has been injured, irritated by infection or resorbed by interference with its blood supply.

Bozzi, in Italy (1934), pointing out that most descriptions of the internal auditory artery are incomplete and insufficient, has recently reported his personal investigations conducted in the Anatomo-Pathological and Clinical Oto-Rhino-Laryngological Institute of the University of Milan. The work was carried out on 105 cadavers, including sixty-eight males and thirty-seven females. The following anatomic behavior could be demonstrated: (1) In forty-seven cases (thirty-one men, sixteen women), the artery originated on both sides from the basilar artery; (2) in twenty-three cases (thirteen men, ten women), it was derived on the right side from the basilar artery, on the left side from the anterior inferior cerebellar artery; (3) in sixteen cases (eight men, eight women), it came on the right side from the anterior inferior cerebellar, on the left side from the basilar artery; (4) in nineteen cases (sixteen men, three women), it originated on both sides from the anterior inferior cerebellar artery. The caliber of the internal auditory artery is very variable; it is smaller when it is derived from the anterior inferior cerebellar, but the opposite may also be the case. In these circumstances the internal auditory artery gives off collaterals which pass towards the domain of the anterior inferior cerebellar artery. In a general way, the internal auditory artery often supplies also the pons, the bulb, the cerebral peduncles, with collaterals. The internal auditory arteries of both sides may also differ from each other. An apparently new observation is the following: The internal auditory artery in the first place passes close to the eighth nerve, then forms a loop backwards shortly before the internal auditory meatus and gives off collaterals into the domain of the anterior inferior cerebellar artery; only a fine vessel of apparently constant caliber passes with the nerve to the labyrinth. An actually double labyrinthine artery was found by the observer in only a single instance.

VI. VASOMOTOR MECHANISM.

The essential causative factor in otosclerosis is defined by Gray (1934) as a slowly progressive failure in the function of the vasomotor reflex of the organ of hearing as a whole. The vasomotor system, which governs the blood supply to the auditory organ, from the external meatus to the cerebral arteries, begins to fail before its time; consequently all the tissues concerned in the function of hearing lose their blood supply to a certain extent. The structures of the organ are not sufficiently nourished to function adequately. Fibrous tissue in the region of the oval window is a degenerative process, with no inflammatory activity, and is due to the deprivation of the extra blood supply to the bone where it is subjected to stress by the movements of the stapes in response to sound vibrations.

Clinically the loss or sluggishness of the tympanic vasomotor reflex, the loss of low notes, the negative Rinne test and continuous tinnitus all suggest that some defect in the vasomotor system of the organ of hearing is the fundamental factor in the causation of otosclerosis. The ear affection known under this name is accordingly equivalent, in Gray's opinion, to a failure of the vasomotor reflex function of the organ of hearing. This explanation has so far found few adherents and many sceptics. Such an attitude is perhaps not surprising in view of the fact that the old assumption of an absent cerebral vasomotor supply has hardly been questioned in the past. According to Bayliss (Vasomotor System, 1923), the cerebral circulation is entirely dependent on the general arterial and venous pressure.

The hereditary transmission of a lessened resistance of the autonomous and sympathetic nervous system was pointed out by W. Sohier Bryant (1913) as the responsible factor in otosclerotic heredity. The anatomy of the sympathetic system is not yet entirely understood, and it is surprising to note how little progress has been made along this particular line of inquiry. Bardeleben (1906) states that the vasomotor nerves of the sympathetic form plexuses around the arteries, veins and capillaries, and from these perivascular networks arise ramifying lateral strands, which are apposed to muscular fibers of the vascular wall.

As pointed out by Delamere and Tanasesco (1906), whose investigations were carried out in the anatomical laboratory of the Paris Medical Faculty, the literature furnishes only scanty infor-

mation on the vessels of the sympathetic, more particularly those of the head sympathetic. The arterioles of the ophthalmic, sphenopalatine, otic and submaxillary ganglia were briefly described by Kurt Bartholdy in 1897. The scantiness of information is undoubtedly accounted for by the difficulty of injecting and dissecting the very fine and rather variable arteries of the regional sympathetic. By means of a careful technic of their own, the French investigators were enabled to obtain results concerning the origin and course of the arterioles which supply the ophthalmic, sphenopalatine, otic, submaxillary and sublingual ganglia. With special reference to the otic ganglion they state that according to Kurt Bartholdy and other anatomists, the artery of this ganglion is a branch of the middle meningeal. As shown by their own investigations, this arteriole is almost invariably derived from the trunk of the pterygopalatine or superior palatine artery, and is distributed over the internal aspect of the otic ganglion. Each of the ganglia of the head sympathetic receives at least one nutrient arteriole. Multiple ganglionic arteries form anastomoses at the periphery of the nerve center. The arteries of a given ganglion of the sympathetic are and always remain independent of the arteries of the other ganglia. The head sympathetic, according to them, is characterized by dissemination of the nerve centers and independence of the vascularization.

The mechanism of control of the blood vessels is governed by the vasoconstrictor nerves, which are exclusively derived from the sympathetic system (Bayliss, 1923), and are distributed to all parts of the body. Vasomotor sympathetic syndromes, cerebral, auricular and visual, were discussed in 1923 by Laignel-Lavastine, who had previously called attention to the considerable influence of disturbances of the sympathetic on the brain. Credit is given by him to Lermoyez who, in 1919, interpreted labyrinthine angiospasm as pain of the cochlear nerve (tinnitus), showing it to be a special instance of the vascular crises of Pal; also that just as spasm of the retinal arteries produces temporary amaurosis, spasm of the internal auditory artery with its two cochlear and vestibular branches gives rise when complete, to Ménière's triad, namely, deafness, vertigo, aural tinnitus. Spasm of the vestibular artery elicits an attack of vertigo, without concomitant auditory disturbances. Spasm of the cochlear artery gives rise to crises of sudden and transitory deafness with severe aural tinnitus, without vertigo. This semi-syndrome of Ménière is much more imperfectly known than its exclusively vertiginous masked form. In the case of a woman with Raynaud's syndrome, Lermoyez (1919) was enabled to observe a typical angiospasm of the

anterior labyrinth. The mechanism is exactly the same, in the two localizations, digital and labyrinthine. Gradual occlusion of the internal auditory artery induces progressive anesthesia of the ear, namely, deafness. When the spasm is suddenly released, the blood again rushes into the labyrinth, and this abrupt inflow (which in the asphyxiated fingers gives rise to pain) here causes at the same time the special pain of the cochlear organ, namely, aural tinnitus, together with disturbance of the vestibular organ, namely, vertigo; it moreover causes the disappearance of ear anesthesia, namely, the removal of the deafness. For this reason, this interesting contribution was published under the paradoxical title: "Le vertige qui fait entendre" (The vertigo which restores hearing), with the subtitle "Labyrinthine Angiospasm." The vertiginous syndromes of the labyrinth were described on the basis of some illustrative cases, by Caliceti, Otorhinolaryngological Clinic of the University of Bologna (1933). The syndrome described by Lermoyez (1919) consists in unilateral, gradually supervening deafness, which subsides again within a few hours, under severe vertigo and subjective ear noises. The cause of this phenomenon is sought in a spasm of the internal auditory artery; on release of this spasm, vertigo is induced through the abrupt return of the blood. In the Ménière syndrome, on the other hand, the vertigo ushers in the clinical picture, and the vessels are said to be congested. Pende (1909) considers both syndromes as signs of a disturbance in the vegetative nervous system.

In the Dalby Lecture, delivered by Albert A. Gray in May of 1934, on the subject of the ototclerosis problem, the essential causative factor in the disease was declared to be a slowly progressive failure in the vasomotor reflex of the organ of hearing as a whole. The resulting curtailment of the blood supply means insufficient nutrition for the structures of the organ, with all its sequelæ.

Changes in the Auditory Nerve.—Otosclerosis, according to A. A. Gray, is a degenerative process affecting the organ of hearing as a whole; the pathologic changes in both the labyrinth and in the cochlear nerve are manifestations of this process and the cause of the clinical symptoms. The diminished secretion of cerumen, sluggish vasomotor reaction in the blood vessels of the tympanic membrane and diminished sensitiveness of this membrane, which are characteristic of otosclerosis, as well as the nature of the pathologic changes in the bony capsule and the cochlear nerve, suggest that the underlying factor is in the vasomotor arc that controls the nutrition of the organ of hearing as a whole. In four cases of otosclerosis which were studied by him with special reference to pathologic changes in

the auditory nerve, such changes were plainly demonstrable besides bony fixation of the stapes. In the early stage of the disease, the medullary sheath is the first to undergo degeneration, as shown by the breaking up and loss of the neurokeratin filament, followed by breaking down of the neurilemma, resulting in the formation of large spaces through coalescence of several adjacent nerve fibers. In his specimens the axis cylinder finally revealed a tendency to disappear, although some axis cylinders persisted even in the most advanced cases. In a far advanced case of senile deafness, which was studied for comparative purposes, the axis cylinder survived. In two cases under his observation deafness supervened before the stapes became fixed; the deafness in such cases must be attributed to the pathologic changes of the nerve. In the observer's opinion, these changes explain certain symptoms of otosclerosis, especially paracusis Willisii and aural tinnitus. Normally, the axis cylinder of a nerve fiber is insulated by the medullary sheath and probably also to a certain extent by the neurilemma, so that under normal conditions nerve impulses cannot pass from one nerve fiber to adjacent fibers. The medullary sheath and the neurilemma also protect the axis cylinder against the products of metabolism in the surrounding tissues which might irritate it. With the medullary sheath damaged or destroyed the axis cylinder is exposed to such irritation, which in the case of the cochlear nerve would result in subjective sensation of sound, namely, aural tinnitus. This would also account for the cases of otosclerosis in which tinnitus is the first sign of the disease, since Gray's findings indicate that degeneration of the medullary sheath occurs early in the course of otosclerosis.

The existence of symptoms referable to vasomotor disturbances in some otosclerotic patients was mentioned by Mayer in 1911.

The vegetative regulation of the peripheral vestibular apparatus has recently (June of 1934) been described by Professor Rudolf Leidler, Vienna. The extremely complicated structure of the labyrinth, in which tissues of the most variegated type meet and commingle—liquids, gelatinous matter, connective tissue, bones, nerves, simple and highly differentiated epithelia—requires the vegetative system to maintain the entire apparatus in perfect condition to discharge its manifold duties. Experimental proof is already available showing that the vegetative system is directly concerned in the mechanisms of the inner ear. The influence of the vegetative nervous system on vestibular irritability has been demonstrated [Cantele (1933), Cantele and Grahe (1932)]. Spiegel (1932), in discussing the influence of the vasomotors in particular on the function of the

internal ear assumes a threefold dependence on the part of the vegetative nervous system: dependence on the state of contraction of the afferent artery, on the permeability of the vascular walls and on the fluctuations of the blood pressure.

The supremely difficult task undertaken by Leidler aims at an explanation of the vegetative regulation of the peripheral vestibular apparatus. The student is reminded that there is no part of the body that is not reached by fibers of the autonomous nervous system, if only by way of the blood vessels. Sympathetic fibers also enter the labyrinth with the blood supply. Leidler's anatomic data follow in extenso, being probably of fundamental importance for the otosclerosis problem; certainly from the viewpoint of the vasomotor theory.

The arteries of the labyrinth originate from the internal auditory artery, a terminal artery derived from the basilar artery. It enters the internal auditory meatus with the trunk of the acoustic nerve and divides into the vestibular artery and the common cochlear artery. The former passes with the utriculo-ampullary nerve and supplies the macula utriculi and the cristæ ampullaris of the upper and lateral semicircular canal with a dense capillary network. It furthermore forms capillary loops around the initial segments of the semicircular canals and around the upper portions of the utriculus and sacculus. The common cochlear artery divides into two branches, of which the arteria cochlearis propria belongs exclusively to the cochlea. The vestibulo-cochlear artery sends a branch, with the posterior ampullary nerve, to the crista of the posterior semicircular canal; a twig passes to the macula sacculi. It furthermore supplies with numerous small branches the region of the vestibular cul-de-sac, the lower surface of the sacculus and utriculus, the walls of the crus commune and the other semicircular canals.

Aside from the cranial arteries, the labyrinth also receives blood vessels from the middle ear. Vascular connections were found between the tympanic cavity by way of the round window and the ampulla of the posterior semicircular canal and also between the mastoid antrum and the horizontal semicircular canal. The arteries of the middle ear are for the most part derived from the external carotid, a few small twigs coming from the internal carotid.

From the cervical sympathetic, ganglion cervicale superius, fine nerve fibers pass bilaterally to the internal carotid, weaving around the vessel and passing with it into the interior of the skull, which is likewise reached by such fibers with the vertebral arteries from the stellate ganglion. The two carotid plexuses become inter-related in

the arterial circle of Willis, so that also on unilateral stimulation of the sympathetic, the innervation of the vessels of both hemispheres can take place in the same sense. From these plexuses the vasomotors of the labyrinth vessels are claimed to be derived (Leidler, 1935). Sympathetic fibers have been demonstrated, although only in the arterial wall. The sympathetic nerves which supply the vessels of the middle ear are probably derived from the tympanic plexus. With the caroticotympanic nerve, this plexus receives sympathetic fibers from the sympathetic plexus of the internal carotid. It is not positively known, but entirely possible, that parasympathetic fibers also reach the labyrinth by this route. Aside from the blood vessels, an autonomic nerve supply of the labyrinth may theoretically occur also in a different manner, namely, by way of the ganglion of the vestibular nerve. In continuation of his work along this line of inquiry, Leidler gives a survey of the available essential material, in the form of anatomic, physiologic and clinical data on the influence of the vestibular apparatus on the vegetative system. With special reference to the action of this apparatus on the vascular system it has been shown to induce lowering of the blood pressure, which probably originates by way of the vasomotor center in the medulla oblongata. In this sense, the vestibular nerve may be said to act as an antagonist of the cervical sympathetic, in so far as the latter causes vasoconstriction; the labyrinthine vascular tonus would accordingly be of parasympathetic character.

The existence of an impairment of the vegetative nervous system in otosclerosis has been observed by Muck (1932), in whose experience, since 1925, the application of the adrenalin probe test in all patients with typical symptoms of otosclerosis gave rise to the "white streak," namely, a reaction indicative of a pathologic vasomotor reflex. This vasomotor reaction to the adrenalin probe test is peculiar to otosclerosis and indicates a vasomotor disturbance in the domain of the internal carotid or the auditory artery. Vasoconstrictor phenomena of the auditory artery have been demonstrated during caloric stimulation of the labyrinth by Muck (1933), who on the basis of his observations feels justified in assuming a vestibular sympathetic stimulation, in conformity with Kobrak's (1932) interpretation of subjective vestibular symptoms.

On the basis of experimental investigations, Motoji Ozawa (Japan, 1934) has recently demonstrated that the functional loss of the cervical sympathetic, in guinea pigs, leads to retrogressive changes of the auditory organ. These changes were found at the nerve end apparatus and the striæ vasculares of the labyrinth. Atrophy as well

as further degeneration of the nerve end apparatus were shown in both rabbits and guinea pigs. The changes were noted predominantly on the side of the paralyzed cervical sympathetic, but to a less degree appeared also on the other side. Writing from the Kioto Medical Academy, Ozawa regards it as probable that also in man pathologico-anatomic changes should eventually be taken into consideration in the presence of functional disturbances of the cervical sympathetic nerve.

Disturbances of the circulation, vasomotor disturbances, are credited by Gottlieb (1932) with etiologic importance in otosclerosis. He deems it possible that the heredity of the disease depends upon the hereditary differences in the circulation of the labyrinth capsule. As a forerunner of the modern circulatory, vasomotor, sympathetic explanation of otosclerosis, W. Sohier Bryant, nearly three decades ago (1908), pointed out that otosclerotic changes are dependent upon vascular disturbances affecting the regional blood supply, with resultant trophic changes. Among other points, attention was called by him to the particularly complicated arrangement of the tympanic plexus of sensory, motor and sympathetic nerves. (See "Otosclerosis," Volume I, "Influence of Local Conditions," p. 311.)

Pressure fluctuations in the vessels have been called upon by several observers for the explanation of certain labyrinthine phenomena in the neuroses. A "vasogenic labyrinthine hemiplegia," was described by Kobrak (1932), affecting the internal ear entirely or in part. On the basis of the view that the tinnitus in otosclerosis is due to a vasoconstrictor neurosis, Zimmermann (1930) favors the administration of caffein or theobromin. A modification of the labyrinth capsule through medicinal agents with an action on the vasomotors was investigated by Terracol (1933), with special reference to the action of adrenalin and extracts of other endocrinic glands on the labyrinth function. He claims that hyper- as well as hypoirritability of the labyrinth can be restored to the normal standard by peroral administration of adrenalin or very rapidly through intravenous injection of suprarenal extract.

The labyrinthine system and the vasomotor and respiratory reflexes are discussed in an extensive contribution by Cantele in Italy (1933), and Proby in France (1933) describes a vasomotor syndrome of the labyrinth, including many of the vestibular disturbances without definite pathologic changes: "Whatever the cause, all may be traced to a circulatory disturbance."

VII. NERVE MECHANISM: CORTICAL, CENTRAL AND NERVE LESIONS.

Otosclerosis of Central Origin and Changes in the Nerve Tract.—On the basis of extensive studies, Yearsley in England (1933) has arrived at the conclusion that the starting point of otosclerosis is in the brain rather than in the ear. According to him, the blood changes due to the chemical poisons manufactured in the intestinal tract give rise to pathologic alterations in the cortex of the temporosphenoidal lobes; these changes, which involve the pericapillary lymphatics, result in degeneration of the cortical cells of the auditory centers. The characteristic changes in the labyrinth capsule are likened by Yearsley to those of rheumatoid arthritis and certain other bone affections, being of the nature of trophic changes due to nutritional disturbances. A combination of therapeutic measures is accordingly advocated by him in the treatment of otosclerosis.

The apparent necessity for a complete study not only of the temporal bone but also the brain, including the auditory nerve tract to the cerebral cortex, was pointed out by Drury, in 1929, and Yearsley at the International Congress of Oto-Rhino-Laryngology in the preceding year had stated that the primary and essential change of otosclerosis occurs in the cortex of the temporosphenoidal lobe, i. e., the organ *by* which we hear (the brain) rather than in the organ *with* which we hear (the ear). His experience with the insidious and progressive course of otosclerosis in over thirty years suggests a slow poisoning of the cortical cells in the "cerebral auditory apparatus" rather than progressive changes in the ear itself. For the poisoning of the brain cortex, chronic intestinal intoxication (auto-intoxication) is held responsible by him, and this condition accounts for the advance of the disease through increased toxic activities as well as for stationary intervals through temporarily increased resistance.

According to Gottlieb (1929, 1932, 1934), it is very likely that the lesion in the hearing organ occurs first and that the bony lesion of the labyrinth capsule develops subsequently. This conclusion is based on a study of postmortem findings in early and more advanced cases of the disease. It is presumed therefore that the bony lesions occur independently of the degenerative process in the nerve, although due to the same cause, which may be a disturbance of the neurovascular mechanism. The assumption is permissible that the characteristic structure of the cochlea is transmitted from the ances-

tors, the cochlear blood supply varying greatly in different individuals. In some persons the terminal vessels are devoid of anastomoses, whereas others have numerous anastomoses. The former are much more susceptible to toxic and nutritional damage. The pathologic changes in the labyrinth capsule in otosclerosis appear later than the changes of the auditory nerve, as demonstrated by Gottlieb's autopsy findings; but both these changes are produced through neurovascular disturbances.

The repeated observation to the effect that after the performance of the Sourdille operation the hearing is improved to the same degree in the nonoperated ear as on the operated side would seem to point to circulatory influences by way of the brain. The experimental findings of Wittmaack (1930) point in the same direction.

Ruf, in his study of central disturbances of hearing (1934), points out that in their course to the dorsal and ventral cochlear nuclei, the acoustic fibers divide into three bundles, most of the fibers of which cross and pass by way of the lateral tract medial to the geniculate body to the temporal lobe, widening out and terminating in the transverse temporal gyrus.

A very recent contribution by M. de Crinis (1934): "Anatomy of the cortex as a basis of the physiology and pathology of hearing brings the demonstration of Cajal acoustic cells hitherto unknown, in the temporal lobe, the internal geniculate body and the acoustic nucleus. The transmission of sensory (auditory) impulses to the higher psychologic centers of consciousness is discussed.

Histologic evidence of otosclerosis, in both labyrinth capsules, and bilateral labyrinthitis, was noted in a case of geniculate ganglionitis (Hunt's syndrome), by Maybaum and Druss (1934), whose patient, a man of fifty-one years, gave a history of diminution of hearing for the past one and a half years, but otosclerosis had not been suspected clinically.

A paper published by Albert Gray, in 1933, under the title "Two Cases of Acusticus Tumors, with Clinical and Pathologic Reports," makes mention of bilateral typical otosclerotic areas in the labyrinth capsule. The spiral ganglion was affected in both these cases as well as in a similar previously reported observation. The organ of Corti was normal, notwithstanding the marked degeneration of the ganglion in two of the cases.

Pathologic Changes in the Auditory Nerve in Otosclerosis.—In the session of the Royal Society of Medicine, Section of Otology,

London, March, 1932. Gray discussed pathologic changes in the auditory nerve in otosclerosis and their significance clinically, especially with regard to paracusis Willisii. In his work on otosclerosis, published fifteen years previously (1917), he emphasized that although no changes of the auditory nerve were demonstrable in these cases, such changes could nevertheless not be entirely excluded. Meanwhile, the microscopic technic has been improved, and his recent investigations confirm his former assumption. The diagnosis in four cases of otosclerosis was certified by the microscopic demonstration of stapes ankylosis. In the first stage of the nerve changes, degeneration of the medullary sheath is seen, followed by destruction of the neurilemma. The axis cylinder is the most persistent. This anatomic fact and the outcome of modern physiologic investigations, in Gray's opinion, furnish an explanation for paracusis Willisii in otosclerosis. Summarizing, Gray points out that in otosclerosis there is a degeneration of the cochlear nerve fibers, manifesting itself first in the medullary sheath, then in the neurilemma and later on in the axis cylinder. This process takes place independently of the stapes fixation or osseous change of the labyrinth capsule and probably precedes both. Deafness supervenes, in consequence of the degeneration of the nerve fibers, before the stapes has become fixed. The clinical picture of otosclerosis is for the most part produced through the degeneration of the cochlear nerve and only to a minor degree by stapes fixation. The latter merely aggravates the existing hardness of hearing and is the cause of the prolonged bone conduction. The diseased condition of the nerve is responsible for the paracusis Willisii, the aural tinnitus and also in a large measure for the impairment of hearing. The diminished secretion of cerumen, in the auditory meatus, the sluggish vasomotor reaction and the associated lowered sensitivity of the tympanic membrane, the bony changes in the labyrinth capsule and the degeneration of the cochlear nerve, are all independent of one another and are not related as to cause and effect. All these changes are presumably caused through a common factor, which in all probability is to be sought in the vasomotor system, as presiding over the nutrition and governing the structures of the auditory organ. The changes in the various tissues are not inflammatory, but are all of degenerative character and may occur to a variable degree as well as in different parts of the auditory organ in individual cases. It is for this reason that the clinical picture varies in such wide limits. Gray has long maintained that otosclerosis is a degenerative process involving the auditory organ as a whole and is due to an inherent defect in the neurones concerned in the function of hearing, including the neurones of the vasomotor system, with the resulting nutritional in-

sufficiency and osseous changes in the bony capsule of the labyrinth. The capsular changes and the alteration of the cochlear nerve, which are responsible for the clinical symptoms, are to be interpreted as manifestations of the degenerative process. The nature of the osseous and nervous changes suggests an underlying cause in the vasomotor arc that governs the nutrition of the organ of hearing as a whole.

The Section dealing with the vasomotor therapy of otosclerosis contains additional information along this line of inquiry.

VIII. ENDOCRINOLOGY.

The anomalies of internally secreting glands which have been repeatedly described in otosclerosis and actually do occur with deafness, are not specific for otosclerosis and show no special type, occurring in variable combinations and without constancy, so that they can be considered only as part manifestations of a degenerative state, but not as causative factors of the ear disease, Bauer and Stein (1924-1925). Up to a certain degree, sex may be assumed to modify the form of manifestation of a constitutional inferiority of the auditory apparatus. According to the findings of these writers, males are more apt to express a constitutional inferiority of the auditory organ in the form of progressive labyrinthine hardness of hearing, whereas females more frequently reveal it in the form of otosclerosis. In those cases where pathologic symptoms on the part of the endocrine system coincide with otosclerosis—a typical constitutional degenerative ear disease—three possibilities enter into consideration: First, there may be a purely accidental coincidence of the two anomalies. Next, the degenerative state may form the supra-ordinated common basis of the phenomena. Finally, the disturbance of the internal secretory system without representing the actual cause of the ear disease, may induce or determine its onset and modify the course of a pre-existing aural affection.

The behavior of the ear, in the presence of thyroid dysfunction, as observed in cretinism and myxedema, has been discussed and illustrated by Alexander (1929), on the basis of long continued personal investigations. Hardness of hearing is extremely common in cretins, hardly one-fourth of whom possess normal hearing. The etiologic relations between hypothyroidism and the auditory organ or its disturbances, respectively, have not yet been positively ascertained. The fact that in cretinism, the same changes are sometimes found in the internal ear capsule as in otosclerosis, an affection typically associated with heredity, indicates that on the soil of congenital aural changes, endocrinic disturbances act as a determining pathogenic factor and that heredity sometimes plays a part also in the ear affections of cretins.

Otosclerosis is known to supervene in various physiologic and pathologic changes of the female sex organism. All the concomitant alterations on the part of the other endocrinic glands are not necessarily always identical. The time has not yet come to decide which endo-

crinic etiology can be established in most of the cases of otosclerosis. Briefly stated, a correct endocrinic diagnosis and therapy can only be entirely individualistic, in conformity with the deficiencies and requirements of a given case. The normal activity of the organism demands the normal function of the internally secreting glands. When this function is altered, no matter whether increased or lowered, the finely adjusted interglandular balance is disturbed and the organ which is under the influence of its special gland will become damaged. The existing condition requires accurate determination in every single case.

Commenting on the behavior of the internally secreting glands, in a series of 1,000 cases of chronic deafness Drury (1929) states, with special reference to otosclerosis: "The endocrinic glands are among the powerful regulators of the levels of the body metabolism. In conditions of functional failure, lowered basal rates are invariably found. When these are associated with a loss of aural acuity, for which no infective or other direct or mechanical cause can be demonstrated, it has seemed a fair presumption that the hearing failure might equally be a result of lowered metabolism deriving directly from the endocrine condition. Experience has shown this to be the case in a very appreciable percentage of true otosclerotics. It follows as a corollary to this postulate that other and nonendocrine agencies producing lowered metabolic rates may equally affect the acuity of hearing as an indirect end result."

Further inquiry into the otosclerotic problem must be conducted in the domain of endocrinology, according to Simeoni (1929), whose extensive animal experimentation (partial thyro-parathyroidectomy) led him to the conclusion that the endocrine system alone can explain and account for many facts and multiple disturbances met with in otosclerosis.

As pointed out by Lenart (1934), the morbidity relations render internal secretory relations of otosclerosis probable: Of Leicher's (1928) 186 cases, the first signs of the disease in over 50 per cent (103 cases) concern the first years of sexual maturity, from fifteen to twenty-five years, and not one before maturity. No less than 71 per cent were of the female sex. Pregnancy, puerperium and climacteric, are known to exert an unfavorable influence upon the otosclerotic process. In the sequence of the various endocrinic glands which have been taken into consideration for the onset of otosclerosis, the parathyroid function has naturally taken its turn. Eventual hyper- as well as hypo-parathyroid genesis of otosclerosis must here be con-

sidered. The occurrence of latent tetany in otosclerosis has been observed, and roentgen treatment has been proposed with alternate irradiation of the parathyroid glands and the otosclerotic focus. No notable results were achieved by means of this therapeutic method or with ultra-violet irradiations of the body (antitetanic action). In order to permit conclusions ex juvantibus, it is necessary to decide in the first place in the case of a favorable outcome, if the roentgen rays in the utilized dose exert a furthering or an inhibitory influence on the parathyroid function. Since the treatment with organic extracts from ovaries, suprarenals, thyroid, etc., sometimes also medication with nonspecific remedies, may be accompanied by a transitory favorable effect, a premature conclusion as to a causative connection between parathyroid function and otosclerosis must be rejected. (Leicher.)

A study of the pancreatic function in twenty-one cases of progressive deafness, including nine cases of otosclerosis and twelve cases of nerve deafness, was carried out by Gottlieb (1931-1932) who, on the basis of the findings in seven otosclerotic patients with defective pancreatic digestion, is inclined to assume a causative relation between the pancreas and the loss of hearing. Otosclerosis is defined by him as a form of constitutional deafness, preventable and curable within certain limits.

The explanation of otosclerosis is sought by Sprunt (1930) in a congenital inferiority of the auditory apparatus, frequently associated with a congenital inferiority of the endocrinic system. In his opinion there is no necessity or justification for assigning to the endocrinopathy an etiologic rôle in the development of tuberculosis.

Working in the Voss Clinic for Ear, Nose and Throat Diseases in Frankfort-on-the-Main, Hinstorff (1930) determined the basal metabolism in cases of otosclerosis and notes that this ear affection presents the pronounced characteristics of an endocrinic disease.

Among the internally secreting glands, the gonads, more particularly the ovaries, have proved a fertile field of exploration and exploitation, on account of the evident connection of the auditory disturbances with the phenomena of the female sex cycle. (Behavior of the hearing faculty at the time of puberty, during pregnancy, puerperium, lactation, menopause.) The otosclerotic process is probably furthermore favored by the fact that the sex phases induce an alteration of the function of still other internally secreting glands. These pathologic changes of the endocrinic glandular system have been interpreted as concomitant symptoms of a general degenerative

state. The known data are in favor of a complexity of causes, some of which may find an explanation in an endocrinic dysfunction.

Otosclerosis is considered by B. L. Bryant (1932) as one of various otorhinolaryngologic disturbances associated with hypothyroidism and relieved by the administration of thyroid extract, in favorable cases.

Comments on the endocrine foundations of otosclerosis are advantageously based on an instructive contribution by Breitmann (1933), of the Endocrinologic Department of the Leningrad State Institute for Advanced Medical Education. Symptoms of disturbance of the endocrinic system are somewhat more frequently demonstrable in otosclerosis than in other ear diseases, and these disturbances may concern various internally secreting glands. Presumably all the noted changes in the endocrinic system as well as other degenerative changes in otosclerosis are to be interpreted as co-ordinated pathologic stigmata of degeneration. Besides this degenerative change, toxic and infectious processes as well as affections of the nerve centers may primarily be the cause of both phenomena, otosclerosis and endocrinic disease; or second, both phenomena may be entirely independent of each other. Internal secretory disturbances, but also the physiological processes during the various phases of the sex cycle, can undoubtedly influence a constitutionally inferior auditory organ in otosclerosis in a threefold manner: (1) Through alteration of the circulatory relations. (2) Through metabolic disturbances of endocrinic origin which influence the formative and growth processes in the labyrinth capsule. (3) Through toxic effects, which in their turn are referable to the perverted functional activity of endocrinic glands. Breitmann says that in view of the uncertainty of eventual relations between otosclerosis and various internally secreting glands, it is readily understood that the treatment of otosclerosis, from the viewpoint of the internal secretions, has not so far proved satisfactory. Generally applicable therapeutic prescriptions, adapted to every case, cannot be formulated in otosclerosis, for the reason that the constitutional inferiority may concern a great variety of organs and endocrinic glands. This accounts for the fact that thyroid, hypophysial, suprarenal or ovarian products may exert rather favorable effects, at least inducing a subjective improvement of the ear noises in part of the cases, while in other apparently similar cases these remedies fail entirely or may actually aggravate the deafness. The statements of some writers that organic extracts of endocrinic glands (thyroid, parathyroid, hypophysis, ovaries, suprarenals, pancreas) benefit otosclerosis in some cases, does not prove any causative connection of

these hormones with the disease: for as pointed out by Leicher (1929), the improvement of the hearing and the tinnitus may be brought about through nonspecific effects on the blood pressure, the circulation and distribution of the blood, and on the softening or dehydration of the tissues, respectively. None of the available hormones has so far proved sufficiently valuable to be introduced as a generally efficient remedy in the therapy of otosclerosis. On the basis of extensive experience, Breitmann (1933) arrives at the conclusion that there is not and cannot be a uniform etiology of otosclerosis, from the viewpoint of the internal secretions. In the majority of the cases under his observation he was enabled to demonstrate a subfunction of the female gonads (subgenitalism).

One by one, the incriminated glands, after the most careful laboratory research as well as clinical observation, now apparently stand acquitted of primary responsibility; although it is entirely plausible that certain internal secretions may be altered and invested with pathogenic properties through an original metabolic disturbance: It is in this way that a concatenation of several theories, each containing a modicum of truth, may eventually be traced to one common pathogenic factor. Thus it becomes necessary to unravel a tangled skein of fact and surmise.

Many years ago a form of deafness to which women are liable at the cessation of menstruation (probably otosclerosis) was described by Tilt (1853) in his "Elements of Health and Female Hygiene." This deafness occurs in women who have never suffered from rheumatism and can only be explained by taking into consideration the peculiar condition of the nervous system at the change of life. Tilt has also sometimes met with this form of deafness in young women at the period of the first menstruation.

IX. METABOLISM.

Metabolism in Otosclerosis.—The body metabolism, meaning the sum of the chemical changes whereby the function of nutrition is effected, has been the objective of considerable research in the domain of otosclerosis. Brunner (1923) points out that under the influence of a still unknown metabolic disturbance, a dystrophic process in the form of otosclerosis affects the bone and the chondroid supporting tissue of the internal ear capsule. This process develops on the soil of a constitutional and transmissible (by heredity) inferiority. A continued metabolic disturbance will eventually result in an increase of the otosclerotic foci which have been formed, and whose localization is dependent upon the distribution of the nutrient blood vessels.

It is possible that endocrinic disturbances are the ultimate cause of the various metabolic phenomena noted in otosclerosis, but no definite internally secreting gland has so far been convincingly incriminated. However, otosclerosis is now very generally considered, not as a local affection of the labyrinth capsule, but as a general disease with characteristic metabolic changes. To begin with, a diminution of the content of the blood serum in total calcium was pointed out by writers in this country and abroad, but in a much more numerous group of patients under Breitmann's (1933) observation, the calcium content was normal or actually increased. In none of these cases could even the slightest symptoms of parathyroid disease be ascertained. On the basis of clinical experience, such as, for example, the influence of pregnancy, the local otosclerotic change was soon shown to be closely related to the metabolic behavior of the organism as a whole. There is still, however, a dearth of positive facts in proof of the interpretation of otosclerosis as a metabolic disease.

The following chemical changes of the blood have been observed in otosclerosis: A slight lowering of the calcium content in the serum; a distinct diminution of the cholesterin in the serum, down to one-fifth of the normal value; a slight diminution of the blood uric acid; a displacement of the albumin-globulin fraction; a diminished CO_2 content in the serum (sign of diminished alkali reserve); diminished lactic acid in the blood.

A metabolic tendency toward acidosis in otosclerosis is considered as more probable than toward alkalosis, by Behrendt and Berberich (1929). The cholesterin content of the serum was found by

Berberich to be almost invariably distinctly diminished, but Breitmann found it for the most part increased, especially in older patients.

A distinction is made by Chajutin (1930, 1932) between otosclerosis with acidosis and otosclerosis with alkalosis. This difference, in his opinion, explains the failure of certain methods of treatment in some cases, while in others such methods are of distinct benefit. In view of the occasional therapeutic employment of bone transplantation in the treatment of tetany, spasmophilia and bone tuberculosis, in order to establish a calcium balance, six cases of otosclerosis were treated by him with subcutaneous implantation of ox bone (from long bones). In four of the six cases this treatment had no effect. In two cases, with definite symptoms of alkalosis, some benefit was obtained, especially with respect to aural tinnitus, but a slight improvement in hearing distance for the whispered voice was also demonstrable. This mode of treatment is evidently indicated only in cases of otosclerosis with undoubted alkalosis.

Encouraging results were reported by Johow (1930) from the use of calcium gluconate in the treatment of otosclerosis; the tinnitus was very definitely relieved after a few injections of this calcium salt. An intensive "recalcifying" treatment, including the administration of calcium, vitamin D and phosphates (the latter to increase fixation of calcium) was employed with encouraging results and some actual cures (four of sixty-four cases) by Berceruelo (1933).

Mirvish, in an article entitled "Otosclerosis: A Metabolic Disease" (1930), in collaboration with Bosman, found that a substance named by him calcovarin is present in ovarian extract and reduces the blood calcium in a characteristic way in rabbits and in humans. The same substance is present in the suprarenal cortex and probably in the testicles. A substance extracted from oatmeal by Mirvish is apparently identical with calcovarin and has the same effect on the blood calcium. An excess of calcovarin or a deficiency in vitamin D may lead to the production of rickets. Osteomalacia, a closely related affection, may likewise be referred to an excess of calcovarin through overuse of a cereal diet, especially oatmeal. Calcovarin has been shown to exert its effect on the blood calcium by way of the parathyroids, suggesting that rickets and osteomalacia are caused by a parathyroid disturbance, probably a functional hypoparathyroidism. According to the foregoing investigations, otosclerosis with its low blood calcium is the third disease in this category and in his own experience that can be arrested in its course by means of para-

thyroid medication. The actual inter-relationship between the three factors: parathyroids, vitamin D and calcovarin, are still uncertain. The resulting hypoparathyroidism is regarded by him as responsible for otosclerosis as well as rickets and osteomalacia.

In common with other investigators, Hornicek (1930) found a diminution of the blood serum calcium and also a lowering of the alkaline reserve in cases of otosclerosis. Disturbances in the vegetative nervous system, noted in some of the cases, are referred by him to interference with the humoral equilibrium.

In the Escat Clinic (1931) a diminution of the calcium and phosphorus content and of the basal metabolism was observed. In the observer's opinion, instead of being a local affection of the labyrinth capsule, otosclerosis is essentially due to a general change of the blood, the focal disease representing merely a local manifestation of the blood alteration.

The data in the literature on the behavior of the basal metabolism and the calcium and phosphorus content are somewhat confusing and contradictory. Hinstorff (1930), on the basis of extensive studies of the basal metabolism in otosclerosis points out a probable association of the ear disease with an endocrinic disturbance, indicative of a metabolic change in the sense of acidosis.

Blood analyses for calcium, phosphorus and cholesterol were made in fifty-eight certified cases of otosclerosis, as reported by Edmund Prince Fowler (1930), who concludes from his findings that in cases of established otosclerosis no change of consequence can be detected in the blood calcium and phosphorus. The blood cholesterol showed no abnormal variation in these cases. His study of the blood chemistry in his cases of otosclerosis showed blood counts, blood cholesterol, calcium, phosphorus and sugar within normal limits. He points out that this behavior indicates a persistence of the otosclerotic process in spite of normal blood chemistry, but it does not indicate the nonexistence of some anomaly of the blood chemistry at the beginning of the process.

Grahe and Griebel (1932, 1933) carried out ferment studies in otosclerosis in continuation of preceding investigations, in which general metabolic disturbances were demonstrated by them in otosclerotic patients. It was found that the blood serum of otosclerotics dissolves the labyrinth bone to a higher degree than other bones. This was shown through the determination of the calcium and phosphorus content of the serum after twenty-four hours' action of

scraped labyrinth or temporal bone, respectively. In their present work they were enabled to show that the process is not the same with serum and urine, but takes an opposite course, both being apparently due to a ferment action. It was finally shown that a ferment is contained in fresh bone, which leads to a different behavior of the labyrinth and temporal bone toward phosphorus solutions as well as toward blood serum and urine. Attempts at destruction of this ferment were not always successful. The fermentation is not the same in different individuals, nor on different days in the same individual. A definite rule in these fluctuations could not be established.

The Transactions of the International Otorhinolaryngological Congress, held in Madrid, 1932, are enriched by a review of the work being done in America on otosclerosis, in which J. Gordon Wilson gives a survey of the work by Bast on the embryologic development of the otic capsule and its ossification centers; by Davenport on the heredity of otosclerosis, and by Crockett and Aub on calcium metabolism in otosclerosis. (The first two papers are quoted in the respective subdivisions of this book.)

Crockett and Aub experimented with twenty-three cases of otosclerosis in the metabolism wards of the Massachusetts General Hospital. The selected patients were kept for one month on an otherwise adequate, carefully prepared and weighed low calcium diet. In the early cases the calcium intake was maintained at about 100 mg. a day; these patients were also given 100 units parathormone extract daily and later ammonium chloride, an acid-forming salt, designed to "pull calcium from the body." The parathormone was discontinued after about two weeks; the ammonium chloride was given and continued for some time, in many cases for a year. After a month on the strictly low calcium diet, the amount of calcium was gradually increased, but a considerable restriction of calcium below the normal (modified calcium diet) was maintained for a long period —three or four years in most cases. Many of the twenty-three cases showed signs of thyroid dysfunction, and were given thyroid extract, and these patients showed the greatest improvement. Blood calcium and blood phosphorus were normal in all cases; an estimate of the intake and output of calcium showed that in these cases of otosclerosis there was a storing up of body calcium, a "holding on to calcium." Phosphorus and nitrogen metabolism was normal. Nearly all the cases showed a lowered basal metabolic rate, the average, however, being only minus 10 per cent. In this contribution of 1932, Wilson proceeded to the following statements: Under this treatment, the older patients in whom the disease had existed for a

considerable period, showed little or no progression of the disease; their hearing is practically the same as when the experiments were started four or more years ago. Five or six patients who did not continue the diet showed a marked increase in deafness. Under this diet, two patients have been pregnant once and one patient twice, with no increase of deafness, although the diet had to be modified somewhat in the later months of pregnancy. Early cases in which symptoms of otosclerosis had not been present over a year and the amount of bone changes, as judged by the hearing tests was not great, showed definite improvement in hearing, although the aural tinnitus did not entirely disappear. The use of parathormone is not necessary if ammonium chloride is given in sufficiently large doses, 50 to 60 gr. daily for a considerable period.

There is as yet no unanimity with regard to a connection between endocrine disturbances and bone metabolism. The causative character of internal secretory anomalies manifests itself most distinctly in ovarian dysfunction. Presumably the endocrinic disturbance represents merely a partial factor through the creation of a special disposition, to which further injurious elements must be added, in the form of mechanical factors, such as a mild traumatism, to precipitate the outbreak of the disease.

Constitutional Factors.—The constitutional element in otosclerosis is defined by Albrecht (1931) as an exaggerated local susceptibility of the labyrinth capsule to even slight irritation through general metabolic disturbances or endocrinic irregularities; a modified local behavior of the bone (such as fissure formation); a state of chronic hyperemia. The ultimate cause of otosclerosis is sought by him in a faulty heredity, and the disease, in his opinion, does not depend upon internal secretory anomalies. Internal secretory disturbances, however, acquire a contributory or eliciting significance in certain cases.

Otosclerosis is thought to be merely one manifestation of a general abnormal constitution, by Stein (1930). Numerous writers mention general metabolic or endocrinic disturbances as a leading etiologic feature in this disease. In the opinion of Grahe and Griebel (1932, 1933), the explanation of the exclusive involvement of the labyrinth capsule is its different chemical composition as compared to other bones. Notably the calcium and phosphorus content were found to be higher here than in other parts of the temporal bone of the same case (eleven specimens). Their conclusion is that some change in the blood serum is responsible for an increased breaking

down of calcium in the labyrinth capsule, but not in other bones, due to some difference in the chemical composition of the otic capsule. Continued studies of the same investigators concerning the breaking down of phosphorus in the labyrinth capsule, through the action of diluted blood and otosclerotic blood serum, also showed a positive outcome, supporting their contention that otosclerosis is associated with a disturbance of the general metabolism, causing specific changes in the blood and affecting the labyrinth capsule.

The alkaline reserve of the blood was studied by Sanchez-Rodriguez (1931) in twenty cases of otosclerosis, mostly in young adults, fourteen of whom were women. The deafness in all cases had begun at the time of puberty, in pregnancy or during the menopause. Determination of the alkali reserve of the blood invariably showed it to be definitely below normal (acidosis). The differential diagnosis may be assisted by this demonstration.

A disturbance of the intermediary metabolism may be characteristic of otosclerosis and the internally secreting glands have been held responsible. Muck's (1932) experience suggests a metabolic disturbance in otosclerosis, because a change in the reaction to the adrenalin probe test was produced by the omission of all purin containing foods from the diet (prohibition of meat and fish). In fully developed cases of otosclerosis the symptoms were only slightly modified by the adoption of this diet.

Gottlieb (1934) points out that constitutional deafness is bilateral, progressive, may begin at any age, shows an aggravation at puberty and in pregnancy, and is caused by toxic and nutritional disturbances; the majority of the cases show a diminished basal metabolism. Besides families where numerous members are hard of hearing, isolated cases are repeatedly encountered. In otosclerosis the susceptibility to deafness is inherited, though the onset of the disease be elicited through an external factor. The only type of hardness of hearing which is dependent on heredity alone, without an external activating factor, is found in bony fragility. The pathologic changes resemble those of otosclerosis. The assumption is permissible that the characteristic structure of the cochlea is transmitted from the ancestors, the cochlear blood supply varying greatly in different individuals. In some instances, the terminal vessels are devoid of anastomoses, whereas others have numerous anastomoses. The former are much more susceptible to toxic and nutritional damage. The pathologic changes in the labyrinth capsule in otosclerosis appear later than the changes of the auditory nerve—as Gottlieb is enabled to demonstrate

through autopsy findings—but both these changes are produced through neurovascular disturbances. The same percentage of positive family histories is found in hereditary deafness as in patients with endocrinic disturbances. Progressive hardness of hearing must necessarily have a constant irreversible cause, and this condition is met by a dysfunction of the liver and by endocrinic disturbances. Chronic hepatitis, in his opinion, is a frequent cause of hardness of hearing.

The relations between ostitis fibrosa and metabolic changes, according to Tobeck (1933), vary in conformity with the generalized or localized character of the bone disease. In the presence of a new formation of compact sclerotic bone, as in otosclerosis, a diminution in blood calcium is more probable than an increase, which, on the other hand, is to be expected when there is a marked destruction of bone, as in generalized fibrous ostitis with impairment of parathyroid function. Although bone destruction predominates in certain stages of otosclerosis, the otosclerotic foci in the labyrinth capsule are so small that they are not likely to modify the total blood calcium.

The evolution of the syndrome of hardness of hearing, blue sclerotics and bone fragility is due, in Kindler's (1932) opinion, to a general constitutional inferiority of the organism, transmitted to the offspring, according to the teachings of Bauer and Stein (1913-1914, 1924-1925). In these circumstances no definite condition, such as otosclerosis, is inherited, but the offspring suffer from the general organic "inferiority" in its various manifestations. According to Warwick (1931), the so-called hereditary tendency to otosclerosis results from a deficiency in the formation of the temporal bone in the fetus and young infant. This induces a sensitization of the cartilage cells in adult life, rendering them "responsive" to changes in the hydrogen ion concentration of the blood and blood calcium, such as occur in various forms of endocrinic deficiency.

In the presence of the pathologic pigmentation of the cartilages and other tissues, known as ochronosis—a very slowly progressive affection—otosclerosis has been known to occur. In the case of a man of fifty-four years, suffering from ochronosis and auditory disturbances, Brunner (1929) noted a typical otosclerotic focus anterior to the oval window, separated by a sharp wavy line from the remainder of the bone, without stapes ankylosis. A second smaller otosclerotic focus was found at the lateral insertion of the round window membrane. The bone cells of the otosclerotic foci showed no pigment, in stained or unstained sections, although the old internal ear bone in the next environment of the foci presented distinctly pigmented bone

cells. Brunner emphasizes that although a distinct pigmentation of these foci (which were of small circumference, but otherwise had a typical localization and typical structure) was to have been expected, for a variety of reasons, on the basis of pathologic experience. The contrary proved to be the case; the bone cells of the otosclerotic foci were not pigmented, nor was pigment found in the chondroid supporting tissue of the window frame and the annular ligament, although the foot plate of the stapes in its turn distinctly presented pigmented cells. The bone cells of the otosclerotic foci accordingly behaved toward the ochrosonic pigment precisely like the bone cells of the remainder of the skeleton and opposite to the behavior of the periosteal and endosteal internal ear capsule. In view of the efficient blood supply of the otosclerotic foci, there remains only the assumption that in the fully developed otosclerotic focus the metabolic exchange must take place in a different manner from the periosteal internal ear capsule, no matter if active apposition and disintegration processes are or are not demonstrable in the otosclerotic focus. Brunner concludes that in the vicinity of the two windows, namely, at the site of predilection of otosclerosis, the metabolism in the adult takes place differently than in the remaining internal ear capsule, as is shown by the lack of pigment formed from homogentisinic acid in these localities or a formed pigment being rapidly bleached because of intensive oxidation processes. This difference in the metabolic exchange concerns not only the normal kinds of tissue found in these areas, but also regional pathologic tissue varieties, namely otosclerotic foci.

Alexander (1901) considers it beyond doubt that the accumulation of pigment is connected with the activity of the sensory nerve end terminal as such, namely, in the case of the labyrinth with the activity of the acoustic nerve (in the case of the retina with the optic nerve). The pigment of the human labyrinth, as well as in the higher mammals, was investigated by him (1901) in the Vienna First Anatomical Institute. In the human newborn he saw only very scanty pigment in the pars superior; scanty pigment inclusions in the subepithelial zone at the cristæ acusticæ. In the adult, pigment was occasionally found in the intermediate zone of the sinus utriculus posterior and the posterior ampulla; in other cases, pigment was seen in ramified cells around the crista acustica and the macula utriculi. No pigment was found at the semicircular canals. In the pars inferior, pigment inclusions were encountered in two cases in the epithelium of the free saccular wall. In the newborn, ramified pigment cells were found in one instance in the endosteum of the scalæ and

in the axial connective tissue of the cochlea. The same findings were not uncommonly noted in adults. The pigment granules here appear of a light to dark brown color. In the cochlear spiral also groups of pigment cells were found which in part extended along the capillaries, weaving around the vessels with the cellular processes. Abundant ramified pigment cells were found in specimens of different ages at the marginal insertion of the membrana tympanica secundaria. Pigment inclusions are furthermore noted in the stria vascularis varying in quantity and appearing sometimes only in the connective tissue cells of the stria, sometimes in addition also situated between these and even in the epithelial portion of the stria. Rare findings are represented by the occurrence of pigment cells in the cellular layer of the vestibular membrane situated at the scala vestibuli, in the crista spiralis, at the lamina spiralis ossea and the nerve strands of the internal auditory meatus. Not infrequently pigment is found in the vestibular floor, in the form of ramified pigment cells situated in the soft tissue and the superficial marrow spaces. The pigment varies in color from a light to a dark brown, but in the same case usually shows the same coloration of the elementary granules, which are strongly refractive. Pigment is found also in the surroundings of the blood vessels of the bone and even the endothelium which lines the scanty marrow spaces of the petrous bone occasionally presents pigment inclusions. The vestibular floor may be regarded as the site of predilection: Also in man, the vestibular floor is very often found to be discolored and of a dark brown color. The occurrence of pigment about the nerves of the internal auditory meatus is extremely variable. A typical arrangement, but not of regular occurrence, is shown by the pigment in the cochlear spiral.

X. MECHANICAL FACTORS.

The theory of mechanical irritation, propounded by Brühl (1920) and endorsed by others, as a cause of otosclerosis, is strongly supported by the similarity of the otosclerotic focus with fibrous osteitis, the etiology of which was referred by von Recklinghausen to a mechanical stimulus. But the common stimulus eventually accounting for the appearance of the focus at different points of the petrous bone still remains to be determined. The labyrinth capsule, as pointed out by O. Mayer (see bibliography of Otosclerosis, 1928) is especially exposed to mechanical irritation or strain, because of: (1) its complicated configuration; (2) its histologic structure. Evidence of the effect of this strain on the labyrinth capsule is shown, in his opinion, by fissures at the points of greatest strain. The otosclerotic foci develop at the same points and thus represent a biologic reaction, namely, an attempt to form a more solid and resistant bone at the site of the greatest strain. The mechanical relations as well as the statics of the labyrinth capsule and the temporal bone as a whole were analyzed by Mayer, with the following results: This bone is wedged into the base of the skull and has much weight to sustain. The apex being surrounded by vascular orifices covered with connective tissue, it is somewhat movable so that the center of the bone, namely, the domain of the labyrinth, is most heavily weighted. There is reason to assume that the maximal weighting passes along the longitudinal axis of the pyramid. Knowledge of the structure of the labyrinth is equally important for the study of the influence of mechanical weighting. Its very configuration, with large curved surfaces, channels and orifices, deprives it of much resistance against weighting. The same effect is exerted by the peculiarities of the labyrinth bone. Until a far advanced age, the enchondral capsule of the labyrinth contains persistent islands of embryonic cartilage and bone. The structural changes noted in other bones of the body, regeneration of the bone through the ingrowing system of the Haversian canaliculi, are missing in the capsular bone. The capsule undergoes early senile changes, manifested by sclerosis and fragility. The enchondral capsule is normally surrounded by a second periosteal capsule in which active transformation processes are at work, maintaining the elasticity of the capsule. Evidently, on taxation, the brittle internal bone will be the first to give way and split asunder. Briefly, the movable temporal bone harbors a labyrinth capsule of highly complicated shape, with a fragile nucleus and an elastic sheath.

Mechanical stresses play a considerable part in bone development and bone pathology, and have a strong bearing on the structure of the bone. In collaboration with E. Schwall, professor of architectonic statics, Mayer found that the capsule is influenced through the weighting (brain mass, pressure of the lower jaw), as well as through changes in position (pathologico-anatomic changes in the bone, such as ostitis deformans). Cöoperative vibrations due to aging of the bone may be likened to contractile processes in building material: The brittle nucleus, unable to follow the movements of the external layer, breaks and gives rise to microfissures. Mechanical weighting is indicated by the numerous fissures in the labyrinth of the aged. These fissures are situated at very definite points, in conformity with the point of maximal mechanical stresses, namely, around the orifices, and become gradually filled with connective tissue. The cracks or gaps have been noticed by many investigators, but were not always correctly interpreted. No precise data are available as to their time of onset and selective localization. The gaps in the bony labyrinth capsule have been explained through senile changes of the bone; through tension of the enchondral capsule in the course of transformation of the periosteal capsule, and through physiologic or mechanical stresses of the labyrinth. Thus the gaps originate as the result of a misproportion between the demands upon it and the resistance of the labyrinth capsule. Information is available showing that mechanical stresses may be followed by a restricted absorption of old bone and its substitution by young, plexus-like bone. The otosclerotic foci develop regularly at the points of maximal stresses of the labyrinth, such as the windows, the semicircular canals, at the points of entrance into the ampullæ, on the floor of the internal auditory meatus.

The cause consists in the misproportion between taxation and resistance of the bone tissue. This diminished resistance (or increased sensitivity) is dependent upon the constitution and other as yet unknown factors. In consequence of the process, an otosclerotic focus supervenes, namely, a scar of plexus-like tissue, more resistant against mechanical traction, which prevents the further enlargement of the gap. While conceding the inducements of the theory of mechanical irritation, as a cause of otosclerosis, Mayer points out that a mechanical absorption of the bone is hardly conceivable: In the presence of a mechanical cause, absorption would proceed from the site of pressure as far as the bone marrow cavities, which has not been shown in any specimen. The otosclerotic focus, which evidently grows from the periosteum inwards into the depth of the tissues, begins with the absorption of the old bone. As to the genesis of the

otosclerotic process, the causes, in his opinion, may be of general or local character.

According to Leiri (1929, 1934), the mechanical factors surmised by Mayer probably possess no notable significance for the genesis of fractures or fissures described by him. The cause of these fractures is presumably altogether different and in Leiri's opinion, consists in the carotid pulsation (as repeatedly emphasized by him), uninterruptedly and very violently knocking against the apical portion of the pyramid. This factor is efficient in the formation of foci in the vicinity of the carotid knee, but also for the origin of foci in the semicircular canal part of the labyrinth, at the round window and on the floor of the porus acusticus internus. Other significant mechanical factors in the pathogenesis of otosclerosis are the movements of the stapes plate in the round window, which give rise to formative irritant processes in the periosteum and in the bone anterior to the oval window. Another mechanical factor which may be concerned in the formation of the foci anterior to the oval window and in the vicinity of the lateral insertion of the membrane of the round window, is the tension of the basilar strands in the basal cochlear convolution. Further mechanical causes which may bear upon the origin of otosclerotic foci are eventually referable to the increased intralabyrinthine pressure produced by the movements of the stapes plate, as well as the movements of the membrana tympani secundaria. The impetus of the carotid pulse, in Leiri's opinion, is responsible for otosclerosis as well as for fractures or fissures in the vicinity of the apical portion of the pyramid, at the labyrinth windows and in the semicircular canals portion of the labyrinth. According to Leiri, Mayer's demonstration of his fractures or microfissures in aged individuals is not explained primarily through the greater fragility of senile bone, but also in such a way that the efficient causative factor, namely, the pulse of the carotid artery, is stronger at an advanced age due to the increase of blood pressure. In seeking for other local causes, he surmises an eventual effect of electro-chemical tension: The bed of the current is formed by the vas spirale and the stria vascularis; the current originates through the electric tension between the blood (positive charge) and the vascular wall (negative charge). Through the movement of the blood, the negative charge accumulates at the vestibular end of the vas spirale in the vestibular cul-de-sac, while the positive charge accumulates at the apical end of the vessel. As the result of variably strong isolation of the current, electrolysis occurs with eliciting of ions, including calcium ions, which together with the mechanical stresses of the labyrinth capsule is assumed to

favor the formation of otosclerotic foci, especially in the condition where the electric current is confined, or strictured, as it were, in the vicinity of the apertures of the labyrinth capsule. The significance of the cartilage remnants, emphasized by others, is sought by Leiri in the quality of the cartilage as a worse conductor than bone, constricting the bed of the current. The electro-chemical action must evidently be stronger in otosclerotics than in normal individuals, and therefore capable of weakening the labyrinth capsule to a higher degree. This is confirmed by the diminished content of the blood of otosclerotics in calcium, cholesterin and other kations. The dilution greatly diminishes the conductivity of the blood; the current which traverses the labyrinth capsule is proportionately stronger than that in the blood of the stria vascularis; hence the electrolytic disintegration of the labyrinth capsule. A further factor which gives rise to an increase of the electro-chemical action in otosclerosis is seen in the increase of the current potential due to the diminution of the calcium content in the blood.

XI. ANIMAL EXPERIMENTATION.

The labyrinth capsule of rabbits and guinea pigs, which are preferable to rats and mice for experimental purposes along this line of inquiry, was shown by Hafner (1933) to bear a close resemblance to the human type in its development and also in its final fibrillar structure. In both these animals the labyrinth capsule presents three layers, endosteal, enchondral and periosteal; the enchondral layer contains cartilage remnants. Notwithstanding this similarity, however, the existing differences in the animal, as compared to the human organ, must be duly considered in the formulation of conclusions in regard to changes in the bony labyrinth capsule. In guinea pigs the bony labyrinth capsule was studied by Gale and Jaffe (1931) during acute and chronic hyperparathyroidism, induced by the injection of parathyroid extract. In these animals the labyrinth capsule was found to show few or none of the characteristic changes, although the adjacent skull bone presented variable degrees of resorption with evidence of Howship's lacunæ, osteoclasts and fibrous tissue. These findings are explained by the investigators as due to the low rate of metabolism of the guinea pig's bony labyrinth capsule, which is a region of less active bone growth. Much more active bone growth is demonstrable in the labyrinth capsule of normal young chicks and puppy dogs, so that in these species resorptive bone changes and fibrotic lesions can be much more easily produced by suitable stimuli than in guinea pigs.

On the basis of his physiologic and pathologic studies of the parathyroid glands, Simeoni (1929) proceeded to experiment on dogs and rabbits, with partial thyro-parathyroidectomy and hemi-parathyroidectomy, and to watch the resulting effect upon the calcium metabolism and upon disturbances of the labyrinthine capsule. Such changes were demonstrable in the operated animals. The influence exerted by the parathyroids on the calcium metabolism is an established fact and so is the production of changes in the osseous tissue of the periotic capsule through alteration of this equilibrium. However, the conditions obtaining in man can hardly be duplicated in animal experimentation.

Experiments on young rabbits, to determine the effect of parathyroidectomy on the labyrinth, were reported by Borghesan (1930) in Italy. After the onset of symptoms of parathyroid insufficiency the animals were killed at varying periods after the mutilation. The

membranous labyrinth in every instance presented only congestive hyperemia, without other demonstrable changes. The bony labyrinth, on the other hand, showed changes resembling the first stage and the beginning of the second stage of human otosclerosis. In the offspring of the operated animals no changes were in evidence, but the young were very sensitive to parathyroid insufficiency as a result of removal of the parathyroids seven to ten days after birth. The observations are suggestive of parathyroid insufficiency as an eventual factor in the etiology of otosclerosis. In the young parathyroidectomized rabbits, which succumbed to tetania parathyreopriva, the histologic examination showed a very hyperemic bone, as is to be expected at this early age. Microscopic examination showed in one of several femurs of rabbits which had died from tetany a practically complete disappearance of the so-called growth cartilage, confirmed by the microscopic appearance after decalcification. The acoustic, cochlear and vestibular nerves were intact. The spiral ligament was hyperemic, and the same hyperemia was noted in the vestibule and in the membranous semicircular canals, their walls appearing furrowed by congested turgid vessels. The hypoparathyroid state, giving rise to spasmophilic phenomena, manifested itself in the internal ear by the production of hyperemia and a moderate absorption of the calcium substance; changes comparable to the first and in part to the second stage of otosclerosis: osseous absorption, disappearance of osteoclasts. Borghesan (1930) points out the probability of involvement of also the finest nervous structures, resulting in a functional alteration of the ear due to parathyroid deficiency.

Torrini (1934), in Italy, on the basis of those theories which seek the pathogenesis of otosclerosis in a dysfunction of the internally secreting glands, endeavored to investigate experimentally if and to what degree the partial or total removal of the gonads, male as well as female, can exert an influence on this disease. His experiments were divided into two groups, one of eight male and one of eight female guinea pigs. Only young animals, at most four to five months of age, were operated upon, in order to approximate as near as possible the period of evolution when the ear disease begins in man. The two groups were divided into two subgroups, of four animals each, on which Torrini performed unilateral (four) and bilateral (four) orchidectomy, and unilateral (four) and bilateral (four) oophorectomy, respectively. No change was noted in the behavior of the animals during the entire duration of the experiment; all were killed over six months after the operation. From each animal, both petrous bones were removed, fixed in formalin and decalcified in a

5 per cent nitric acid solution (hematoxylin and orange stain). Serial sections were prepared, perpendicular and parallel to the axis of the petrous bone. The serial examination showed a complete intactness of the labyrinth capsule. The chain of ossicles was normal as well as the stapedius muscle. As neither definite pathologic changes nor incipient suggestions of future pathologic development were revealed, Torrini feels justified in the conclusion that the partial or total loss of function of the sex glands cannot be considered, at any rate, as the sole etiologic agent of otosclerosis; at least, in the experimental domain. He accordingly believes that the cause of otosclerosis, if actually referable to faulty internal secretion, must not be sought in the functional change of a single endocrinic gland, but rather in a general dysendocrinia or a pluriglandular complex.

A Japanese investigator, Motoji Ozawa (1934) showed that the functional loss of the cervical sympathetic, in guinea pigs, leads to retrogressive changes of the ear. These changes were found at the nerve end apparatus and the striæ vascularis of the labyrinth. Atrophy as well as further degenerative changes of the nerve end apparatus were likewise demonstrable in rabbits. The side of the paralyzed cervical sympathetic was predominantly but not exclusively affected. Presumably also in man pathologico-anatomic changes should be eventually taken into consideration in the presence of such disturbances of the cervical sympathetic.

Lesions of the labyrinth capsule in experimental acidosis through administration of hydrochloric acid were observed by Cusenza (1931) in rabbits which were dosed with the acid until the alkaline reserve of the blood was greatly diminished and maintained at the new low level. The temporal bone, including the labyrinth capsule, showed a marked absorption, similar to that seen in the initial stages of otosclerosis; similar changes were also observed in other bones of the skeleton. The artificial induction of acidosis in rabbits resulted, in the experience of Krainz (1933), in changes of the entire bony framework, resembling human rickets. The labyrinth capsule, especially the walls of the semicircular canals, presented similar osseous changes; the bony wall of the cochlea was unchanged. The capsular alteration consisted essentially in osteoporosis with formation of new uncalcified bone, with primary involvement of the periosteal layer, followed secondarily by changes of the enchondral layer.

Rats were treated by Aprile (1934), in Italy, with a special rickets producing diet, namely, deprivation of vitamins. On histologic examination, anatomo-pathologic changes were found in the

petrous bone, especially in the labyrinth capsule. These changes at first were expressed as a venous stasis, which was followed by decalcification of the bone. In addition, an active proliferation of the cartilage zones with transformation into osteoid substance was in evidence. These changes, although not entirely in conformity, are nevertheless similar to those of human otosclerosis.

The relation of vitamins A, B, D, and G to otolaryngology was investigated by Cody (1932) in a series of animal experiments. As vitamin D has the property of controlling the mineral constituents of bone, seventy albino rats were experimented upon in order to determine whether or not vitamin D deficiency has any effect on the labyrinth capsule. After three to five months' feeding on a vitamin D deficient diet young rats, about one month of age, were found to have soft temporal bones, and a specific change similar to that at the epiphyseal line was seen in the labyrinth capsule. Rats which received a normal diet for four months after the period of dietetic vitamin D deficiency showed no otosclerotic foci in the middle layers or at the anterior edge of the fenestra vestibuli. Cody concludes that vitamin D deficiency produces no lesion in the rat's labyrinth capsule resembling human otosclerosis. Barlow's (1928) experiments on rats and birds with diet deficient in vitamins A and B led to no changes of any kind in the bony labyrinth capsule and no deafness followed. These findings supplement his earlier experiments which had shown that a diet deficient in vitamin D caused no loss of hearing or definite changes in the bony labyrinth capsule.

Experiments with calcium fluoride administration in lactose to six young adult white mice were reported by Levy in 1928. Six other mice served as controls. The experimentation extended over six to nine months; by this time all the fluoride mice were dead, while the controls with one exception (accidental death) were living. The histologic examination of the bony labyrinth capsule in the poisoned mice revealed in four of the six cases a more bluish stain (with hematoxylin eosin) of the bony capsule; the lacunæ were larger, more numerous, more regularly filled with likewise more deeply stained bone corpuscles. The appearance accordingly was that of calcified cartilage or of young and actively growing bone in adult white mice, as if due to stimulation or irritation, or eventual inhibition or arrest of maturation. On the basis of these experiments as well as the findings of other investigators, the observer assumes that fluorine must be reckoned with as a factor in bone metabolism. Prior to these experiments, he had begun the treatment of otosclerosis with calcium fluoride (1:1000 trituration) in lactose. In spite of the treatment,

the disease progressed, although slowly, in some of the cases, but a few patients were definitely improved. In a later contribution Levy (1934) mentions that in the interval considerable further work has been done on the influence of fluorine on the metabolism of bone. His confirmatory further observations encourage him in the belief that therapeutic resources may finally be developed in the management of otosclerosis, "this unconquered form of deafness."

As pointed out by Tobeck in Germany (1933), even the bony labyrinth can now be modified, along with the rest of the skeleton, by special feeding, by administering metabolic poisons and by injecting hormones of certain internally secreting glands. The resulting changes are of osteodystrophic character and are not typical of otosclerosis. Toxic doses of viosterol were utilized in animal experimentation on rabbits, most of which showed generalized osteodystrophic changes, extending in some cases to the bony labyrinth. While somewhat similar to the changes of otosclerosis, it is conceded by the observer that they are not identical therewith.

The experimental work of Wittmaack on venous stasis as a cause of otosclerosis has been extensively discussed in Otosclerosis, Volume I, pp. 323-328, 1928.

Experimental investigations on circulatory disturbances of the internal ear were carried out by Kohno (1929) in Japan (Medical Academy, Kioto). Embolisms in the domain of the internal ear were produced in rabbits through injection of an infusion of lycopodium seeds in physiologic salt solution into the vertebral artery. The resulting embolisms were found abundantly in the domain of the cochlea, but only scantily in the vestibular region. Sometimes irritative vestibular phenomena supervened after the production of the embolisms, especially when these had occurred only unilaterally. The regressive changes in the labyrinth as a result of the embolisms are irreparable, terminating in degenerative atrophy or ischemic necrosis. The arteries of the cochlea therefore presumably do not anastomose with those of the middle ear mucosa.

Culler (1933) found in his animal experimentation on dogs that plugging the round window fossula reduces both the animal's ability to hear and also the electrical pulses over the auditory nerve. The findings clearly support the "classical" theory of hearing in relation to the round window's function. The utilized gum plugs which touch the round window, in direct apposition but with no pressure, impede normal oscillations and thereby impair acuity of hearing, as the accepted theory of cochlear function would lead one to expect.

XII. PSYCHOLOGY (ACQUIRED DEAFNESS).

No otologist is fit to practice, as pointed out by Fowler (1935), unless he studies each case from the psychologic viewpoint. Often this is the only service he can render. "He will find the social services of the leagues for the hard of hearing of definite value in promoting healthy mental reactions in these patients as well as their general social and economic adjustment. If there is no league in his community he should see to it that one is established. The American Society for the Hard of Hearing at Washington or the local leagues may be used for information and service." Upon the basis of wide experience the author admonishes: "Study not only the psychology of the child but of the parents and family toward the child; the hard of hearing child may be saved much suffering and led into a happy and useful life by patient teachers and parents properly trained."

Deafness in children, as pointed out by Gundrum (1929, 1933), is not as uncommon as is often considered. Those who will later show otosclerosis have not yet attained the age to manifest it. In his experience, in many of his most severe cases, the deafness had not been noticed at home.

A peculiar psychology which seems to predominate in cases of acquired deafness is noted by Wendell C. Phillips (1927), according to whom every handicap in human experience has its psychologic bearings, but none except obvious fatal diseases provokes more despair, hopelessness and depression than defective hearing. In his opinion, loss of sight never depresses its victims like defects in hearing, and he points out that the psychologic aspect of acquired deafness is the result of the more or less rapid destruction of the power of free human communication in business, society, and even in the street and the shop.

After a careful review of the literature, Ruth Brickner (Conference, 1930) found that the mental effects of acquired deafness represent a subject practically untouched by psychiatrists. Emotional maladjustment manifests itself in two fairly typical clinical pictures, according to Menninger (1923): one characterized by depression, the other by suspicion. Depression as well as paranoid attitude permit their interpretation as the result of an unsuccessful fight of the subconscious mind of the afflicted individual against the violation of his personality. A common consequence of acquired deafness is found in a tendency of the deafened man or woman to shun

his fellows and seclude himself; be it because he fears and endeavors to avoid, a fancied withdrawal of others, partly because personal vanity bars him from exhibiting his crippled social attributes.

Extreme cases, fortunately rare, show the two responses typical of the unadjusted personality reaction, namely, subconscious vindictiveness or hatred, and isolation, i. e., voluntary retirement from social intercourse. Many are helped by lip reading, but this often proves an art inaccessible to those deafened in advanced years, notwithstanding all willingness and application. Menninger's classification of the unsatisfactory types of compensation to the particular deprivation complex can hardly be improved and is quoted in extenso in the following: "From a study of the subject I find that there are two common pictures of mental abnormality seen in the deafened. One is a picture of emotional depression, of despondency, feeling of incalculable and irremediable loss, a sense of isolation, of hopelessness, etc. With this there is, of course, much self-depreciation and often fear and anxiety. The other type is one in which the individual becomes suspicious, basing the suspicion on the fact that people laugh at him or say things that he cannot hear which he believes are probably about himself. He comes to think that his deficiency is the chief topic of conversation, and that because of it he is ostracised, persecuted, taken advantage of, and so forth." "These two types may be thought of as those in which the imbalance is self-depreciatory and those in whom the imbalance is self-appreciatory. Both are actually phases of disorientation. The former leads to despondency and the latter to the so-called paranoid attitude (suspiciousness, ideas of persecution, etc.)."

Acquired deafness, according to the authors of "Ears and the Man" (Peck, Samuelson and Lehman, 1926), has characteristic mental results, their observations of many hundreds of so afflicted persons showing that practically all undergo a period of social inadequacy during which there is considerable mental suffering. This period varies in degree and may be temporary, prolonged or permanent. Here a great deal depends on environment and judicious handling. Self-readjustment is not to be expected of the majority of markedly deafened people, who need the sympathy and assistance of experienced social service workers or psychiatrists. Youthful social service workers in particular are evidently imbued with the idea that "rage and hatred" necessarily are the primitive response to the loss of hearing. In the experience of older observers, especially clergymen, Christian resignation to the will of the Almighty often replaces the

primitive response. A slow advent of acquired deafness permits a certain degree of rational accommodation to the loss of hearing.

Gordon Berry (1933) points out that scientifically the otologist is concerned with whether the patient has a nerve deafness or a catarrhal form or whether there is an otosclerotic heredity, and proceeds to a consideration of the behavior changes as deafness progresses through different ages. According to Kulemeyer (1935), the entire character of an afflicted individual may be modified by the loss of hearing. The importance of the human environment is emphasized by Anton (1932), who calls attention to the fact that many persons who have become hard of hearing carry an abundance of old experiences into the later phase of life. On the other hand, by purposeful endeavor and with the help of sufficient remnants of hearing, the connection by speech with cöoperative friends and acquaintances is often well maintained. Suitable hearing instruments may bring about such an improvement of the hearing that the afflicted are enabled to converse at home and abroad and often to enjoy lectures and the theater. In this manner the personality of the deafened may be well preserved. The sympathy and cöoperation of the human environment constitute a very important preliminary condition for the upkeep of activities and interests on the part of the partially deaf. The blind, as a rule, find more sympathy and assistance in this respect than the deaf. The disturbance of social intercourse is a variable quantity in deaf individuals. Anton points out that propaganda is therefore highly desirable for securing a correct guide to social intercourse with the hard of hearing. They should not be addressed too rapidly. Another common error is to try to render words more intelligible by merely shouting; it is also necessary to aim at a more uniform rhythm as well as a distinct articulation. The loss of a specific sense organ like the ear unfortunately cannot be fully replaced and must often be circumvented through complicated mental processes. According to the time of onset of the deafness, a more or less serious impairment of the phonetic perception and expression supervenes, the imperfection depending upon the time of onset of the deafness, the patient's attention, his kinetic adaptability, the educational influence of the environment. The vocabulary of a deafened person, on the average, is directly proportional to the amount of hearing retained since childhood.

According to Anton's interviews with pedagogues and teachers of deafmutes, there is no "psychology of the hard of hearing"; no such psychology has been published, because each case is a law unto itself. Some individuals with more or less total loss of the hearing

faculty have previously enjoyed the full use of all their special senses. Ear disease is known to develop unrecognized for a long time in many cases, so that a number of persons have already learned, consciously or unconsciously, to train their other senses as substitutes, notably sight and touch. The causes of diminished hearing naturally vary in gravity and many affections of the auditory apparatus are curable. A certain variability in the acuity of hearing is induced in many persons through a change of climate, for the acoustic nerve, perhaps also the vestibular nerve, reacts to changes of air pressure, temperature and to strong winds (Anton). Gradually, after months or years, if the impairment of hearing becomes more marked, the first manifestations may be in the lessened perception of music, noises and the phonetics of conversational speech and by an uneven perception of high and low tones. A very musical clinician who suffered from otosclerosis informed Anton that he now enjoyed only such music as he himself produced on his violin. This complaint has often been confirmed in the observer's experience. Some persons who are hard of hearing state that the hearing capacity is diminished by strenuous listening; this is interpreted by Anton as a fatigue phenomenon. In these circumstances, close attention does not always heighten the sensory capacity of the auditory organ, but may appear to lessen it.

The facial expression of the hard of hearing was studied by Muck (1935), on the basis of Sir Joshua Reynolds', the famous deaf painter's, portrait of himself, which admirably shows the characteristic features of this disturbance. The eyes are fixed on the interlocutor's mouth, while the listener's mouth is partly open and the palm of the hand is placed behind the concha of the ear, in order better to conduct the sound waves to the ear. The drooping lower jaw and half open mouth, seen in many persons hard of hearing, are referable to general muscular relaxation and therefore also relaxation of the small muscles around the mouth, due to the prolonged concentrated attention of the listener (Muck).

The loss of auditory perceptions, as shown by Anton, induces a very variable behavior, depending upon the peripheral or central damage of the auditory system. In spite of individual differences, however, all have in common some of the features of a loss or impairment. The acoustic world of those with defective hearing is not only more restricted and circumscribed, but it is different from the world of those with normal hearing. The loss of acoustic impressions in childhood and youth leads to obliteration or noncultivation of large areas of the intellectual horizon. The result is a different picture of the universe. Apperception and association take a different course.

The greater the loss of hearing, the more marked will be the effects. Mental impoverishment follows in proportion to the higher degree and earlier onset of the deficiency.

Children who do not hear well are often believed to be dull and apathetic; partially deaf adults are apt to be more or less depressed and self-conscious. Peculiarities of character, distrust, suspiciousness are often encountered among the deaf, as a result of their misinterpretation of perceptions, often caused solely by the deficiency of the auditory organ or induced by a lack of adaptation and comprehension in the human environment. The hard of hearing are usually anxious to maintain a friendly intercourse with their fellows and establish this intercourse through the eye as well as by gestures. The intense study of the speaker's facial expression is interpreted by Hubbard (1922) as an attempt to find a suggestion of the sentiment conveyed by modulation as well as the meaning of the sentence. The deaf study not the lips alone, but the whole face, mouth, eyes, eyebrows, even wrinkles and dimples, head poise and gestures, thereby searching for sentiment, and they succeed in a marvelous way. They become expert judges of character from that kind of practice. Hubbard continues: "The philosopher falls back on other resources. He can read into the printed or written word a deeper meaning. A keen intellectuality comes from this practice. Solitude is not without compensation. It develops character and a penetrating mind."

Psychologic experience has taught, as pointed out by Anton (1932), that speech is actively stimulated through close attention and interested listening on the part of the audience. In the intelligent hard of hearing this stimulation may give rise to evident animation of their own talk, especially when assisted by an amiable and courteous facial expression of the listener. In this manner are avoided the mental loneliness and introspection so apt to characterize the neglected deaf. Paranoia is a not uncommon phenomenon in unfavorable circumstances, and such reactions were described by Llopin-Lloret (1933) in a woman of fifty-eight years, who had gradually lost her hearing since the age of twenty-five years. Symptoms of mental aberration and paranoia supervened in the course of time. Although deafness may contribute to the onset of such disturbances, the main reason is often to be sought rather in a primary neurotic disposition. The patient in question belonged to a family in which abnormal characters were not uncommon.

The measurement of certain aspects of personality among hard of hearing adults is the title of a contribution by Welles from the

Teachers' Coll. Contrib. Education (1932). Bernreuter personality inventory scales, together with a small special questionnaire, were distributed through organizations for the hard of hearing. The results are based on the 43 per cent returns (225) from these persons and the 28 per cent returns (148) from the control group (normal hearing friends of the hard of hearing). About 88 per cent of the groups were women. The hard of hearing are more emotional, more introverted, and less dominant than the controls, but there is a large overlapping of the distributions. Sixteen items of special differentiating significance are given. Correlations between the inventory score and factors such as number of years deaf, age at loss of hearing, etc., are all small.

The deafened, in order to keep in touch with their environment and to compete with normally hearing persons in the struggle for existence, are in daily need of an abundant store of spiritual strength and endurance. That the influence of deafness on the psyche may be constructive rather than destructive, is illustrated by the tragic loss of hearing sustained by Beethoven, whose genius, will power and idealism triumphed over his infirmity.

XIII. DIAGNOSIS, PROGNOSIS—NEW TESTS.

As pointed out by Watson-Williams (1929), in the diagnosis of otosclerosis the radiography of the petrous bone presents difficulties, in technic and interpretation, so that clinical observation becomes imperative in most cases. A useful tabulation shows the chief points in the differential diagnosis between otosclerosis and catarrhal otitis media. A definite family history or onset in connection with pregnancy is strongly suggestive of otosclerosis. The clinical picture as a whole must be taken into account in arriving at a decision. The following signs and symptoms are utilized by Woods (1929) for the diagnosis of otosclerosis: Slow onset; tympanic membrane normal in shape and color; no improvement on inflation; negativity or less positivity for Rinne's test; raising of the lower limit of hearing. The exact determination of the last named point is of importance, because this test alone is qualitative, all the others being merely quantitative. His observations have shown that the progress of otosclerosis is accompanied by a steady raising of the lower limit of hearing. The pitch at which the patient ceases to hear can be easily and rapidly ascertained by means of an instrument composed of a series of tuning forks, made for him by Riener (in Vienna). This test is of special value in those cases in which only one ear is affected, as shown by the usual tests, to determine an eventual incipient involvement of the other ear.

In the experience of Barnett (1929) otosclerosis is a rare condition as compared with the enormous number of people who are suffering from deafness. The fact, as pointed out by him, that a patient has marked chronic deafness combined with aural tinnitus, with apparently normal eustachian tubes and tympanic membranes, does not necessarily mean that true otosclerosis is present. The following points are the most important in the differential diagnosis of otosclerosis and chronic middle ear deafness: The condition of the tympanic membrane, usually normal in otosclerosis, rarely so in middle ear deafness; the tinnitus, severe and distressing in otosclerosis, absent or negligible in middle ear deafness; rapid onset of deafness in young persons, characteristic of otosclerosis, probably corresponding with the period of bony ankylosis of the stapes, in contrast with very gradual progressive onset usually in older persons, in middle ear deafness; and the different results of treatment in the two types of deafness. It is not possible to state definitely at present that x-ray evidence of osteoporosis in the labyrinth establishes the diagnosis

of otosclerosis and excludes middle ear deafness, or vice versa, yet at the Bath (England) Ear, Nose and Throat Hospital with the technic of Hodgson (1930), it was found that the x-ray picture of the labyrinth was normal in cases diagnosed as middle ear deafness and showed osteoporosis in those diagnosed as otosclerosis.

The best possible radiograms, in the opinion of Hodgson (1930), would not show the earliest changes of otosclerosis around the oval window or in the basal cochlea. His study of radiograms of the labyrinth in otosclerotic cases sometimes revealed changes found only in the presence of otosclerosis, and regarded by him as typical of the disease, in about one-third of the cases. Some slight lack of definition was noted in the basal portion of the cochlea in another one-third, possibly but not certainly pathologic. No abnormality was shown in the radiograms in one-third of the cases. The extent of the bony changes shown in the radiogram was found to have little relation to the severity of the symptoms. While the x-ray is devoid of value in the diagnosis of otosclerosis, except in about one-third of the cases, repeated x-ray examination when the radiogram shows definite bone changes will serve to estimate the degree of change and eventually help to select suitable cases for therapeutic experimentation. Unsuccessful attempts to demonstrate otosclerotic foci in the x-ray picture were also reported by Thielemann (1930).

Soon after the discovery of the roentgen rays, the first attempts were made to investigate the ear in health and disease with the assistance of this promising adjuvant. However, it was not until the remarkable technical advance of the last decades that roentgen diagnosis was officially introduced in the domain of otology. In many conditions, it has now become a valuable and practically indispensable diagnostic adjuvant. Unfortunately, this is not the case with special reference to otosclerosis, in so far as the interpretation of the radiographic pictures is still waiting to be confirmed by histologic control. Meanwhile, lighter patches have been shown in the environment of the cochlea, in otosclerotic patients, and have been referred to absorption of calcium. Initial cases have been claimed to show rarefaction of the cochlear duct, more advanced cases a distinct blurring of the entire labyrinth structure. Even actual otosclerotic foci have been described.

The relative inefficiency of the x-ray as a diagnostic adjuvant in middle ear disease is illustrated by an instructive case which came to autopsy (Fowler Jr.'s case), (1934). The patient died from a brain abscess secondary to petrositis on the right and showed considerable

evidence of bony regrowth in the petrosa and a chronic mastoiditis on the left, which was never made out clinically either by x-ray or by otoscopic examination.

The representation of the chain of auditory ossicles in the x-ray picture was successfully obtained, by means of a new method, by ter Heege (1933).

Direct radio-diagnosis of otosclerosis, as pointed out by Thienpont (1935) and others, does not give constant or reliable results. The ear disease may develop in the presence of any degree of pneumatization. Radiography may reveal a regular pneumatization of the temporal bone, thereby permitting the observer to exclude an eventual adhesive middle ear inflammation and to render an indirect diagnosis of otosclerosis. It is therefore indicated to ascertain the degree of pneumatization in every individual suspected of having otosclerosis.

Steurer (1933) carried out investigations concerning the applicability of x-ray pictures for the diagnosis of otosclerosis. In none of the examined sixty-four radiograms, derived from thirty-two cases of otosclerosis, could otosclerotic foci be positively demonstrated in the labyrinth capsule. On the basis of the roentgen material of otosclerotics the question was further tested as to the existence of relations between the state of pneumatization of the mastoid process and otosclerosis: As 65.6 per cent of well pneumatized, 26.5 per cent of poorly pneumatized and 7.8 per cent of compact mastoid processes were found, the development of otosclerosis is undoubtedly not dependent upon a definite type of pneumatization. Nevertheless, the roentgen picture can be advantageously utilized in the differential diagnosis between adhesive processes and otosclerosis; for if a good pneumatization is found in a doubtful case, this demonstration up to a certain degree contraindicates the existence of an adhesive process, which as a rule develops only on the soil of a strongly hyperplastic mucosa, combined with a marked disturbance or complete arrest of pneumatization.

In this connection, it is of interest that the confrontation of audiograms and roentgen findings in the ear and the accessory nasal sinuses, respectively, led Fowler (1933) to the conclusion that changes in the condition of the ear are regularly accompanied by analogous changes in the diseased condition of the accessory sinuses. This parallelism manifests itself reliably only when the audiogram and radiogram are taken on the same day.

The early diagnosis of otosclerosis is greatly assisted by means of a method devised by E. P. Fowler for the demonstration of hyper-

emia of the mucous membrane in the region of the promontory. The characteristic reddish glow of the promontory in the presence of otosclerosis may be thus rendered visible when the ordinary methods of examination fail to reveal it. This useful procedure consists in slowly stretching and approximating the drum membrane to the promontory, by means of a magnifying focusing pneumatic speculum; a daylight lamp is used. The drum is thus rendered more transparent and its light reflexes are changed, resulting in modification of the background for comparison. The procedure is regarded by its originator as of special value in children and thus aids the diagnosis of otosclerosis at an early age.

No diagnosis of otosclerosis can scientifically be made without progressive deafness, Bezold's triad, normal middle ear and eustachian tubes, according to Nash (1930), who states that in a series of 1,000 cases of deafness, less than 6 per cent were definitely diagnosed as otosclerosis. "The essential features of the pathologic picture are observed and conceded by all; only details are controversial." This statement still remains unquestioned. "That stapedial ankylosis is common in this condition is conceded; that it is necessary to it is denied; that the pathologic site is internal to the niche of the oval window and may spread over the promontory to the round window, or even occu. sporadically throughout the cochlea or petrous bone, must be admitted."

In their recent "Textbook of Otology" (London, 1932) F. W. Watkyn-Thomas and A. L. Yates express the opinion that the diagnosis of otosclerosis cannot be rendered with certainty during life, and that this form of deafness is essentially incurable. As to radiograms which have been described as indicating otosclerotic changes in the periotic capsule, the eventual causation of these changes by the condition histologically recognized as otosclerosis, has not yet been demonstrated, on account of lack of opportunity for pathologic examination of a radiologically studied ear and comparison of the pathologic data with the radiogram.

The contribution by J. S. Fraser (1932), (Edinburgh), entitled "The Clinical Aspect of Otosclerosis," published in the Transactions of the International Congress of Otorhinolaryngology (Madrid, 1932), Section on Otosclerosis, contains much valuable and practical information in condensed form. Fraser divides otosclerosis into five types: (1) Patients with normal drumheads and normal eustachian tubes, with progressive deafness, with or without tinnitus and paracusis; these patients show the Bezold triad on functional examination. (2) Patients with similar signs and symptoms but with slight opacity

of the drumheads. (3) Patients with upper tone limit depressed, lower tone limit raised, negative Rinne and some loss of bone conduction; advanced otosclerosis with some middle and internal ear deafness. (4) Secondary otosclerosis. (a) Patients with progressive deafness with or without tinnitus or paracusis, with drumheads showing results of former middle ear inflammation (scars and dry perforation). In these cases, in the absence of otosclerosis, deafness is not progressive. (b) Patients suffering from progressive deafness with or without tinnitus or paracusis with middle ear suppuration. Microscopic examination in a number of such cases has shown otosclerotic changes in the labyrinth capsule in addition to middle ear suppuration. (c) Patients suffering from progressive deafness with or without tinnitus or paracusis, but with changes in the drumheads and obstruction of the eustachian tubes, indicative of middle ear catarrh. (5) Patients with progressive deafness, with or without tinnitus and paracusis, with normal drumheads and eustachian tubes, with a family history of deafness but with functional tests characteristic of internal ear deafness; positive Rinne, shortened bone conduction, loss of hearing for higher tones—atypical otosclerosis. In some cases of this type pathologic examination has shown otosclerosis involving the capsule of the cochlea without involvement of the stapes.

In order to investigate the clinical aspects of otosclerosis, the British Otosclerosis Committee (1931) sent questionnaires to over 300 otologists, but only 65 replies were received; not every question was answered in these 65 replies. In calculating percentages for each item in the questionnaire for the following report, therefore, 65 was taken as 100 per cent. The findings are as follows: with respect to the examination of the patient: Local, 54 per cent of the replies stated ear wax was usually absent in otosclerosis; only 10 per cent, that it was normal; 46 per cent noted anesthesia of the meatus. Those who answered the question in regard to the flamingo tinge of the promontory had noted it in 32 per cent of cases. In 88 per cent of replies it was noted that the hearing of otosclerotic patients may remain stationary for long periods; in 87 per cent, that otosclerotic patients noticed a loss of adapting power of the ear—failure to understand mixed conversation though hearing one person fairly well.

Concerning tinnitus, the replies showed that 78 per cent of patients with otosclerosis have tinnitus; the character of the tinnitus varied; the sound of steam from a kettle was noted most frequently. Paracusis was noted in only 55 per cent of patients; 39 per cent of otologists have found it absent in the advanced stages of otosclerosis. Pain in the ear was noted as a symptom of otosclerosis in 54 per cent

of replies, but only in a small percentage of cases. The eustachian tubes were found to be patent in 80 per cent; 60 per cent had found them more patent than normal. Vertigo was noticed in 14 to 16 per cent of patients. A feeling of fullness in the ear was noted as a symptom in 67 per cent of replies. General examination: It was noted in 34 per cent of replies that otosclerotic patients suffered from disturbance of the general health; 55 per cent had found mental depression to be common.

Hearing tests: Schwabach's test was employed in 89 per cent of those replying, but percentage results were not given. The Rinne test was employed by all; Weber's test, by 45 per cent; Gelle's test, by 45 per cent, but considered of little practical value; Escat's test, by only 3 per cent. The Galton-Edelman whistle was used more than the monochord. The great majority of replies (69 per cent as compared to 5 per cent) stated that the degree of deafness in otosclerosis corresponded to the raising of the lower tone limit; 92 per cent noted that total deafness had never been found in otosclerosis.

In the thousand cases of deafness studied by Nash (1930), with special reference to the incidence of otosclerosis in the series, a diagnosis of otosclerosis was made only in cases of progressive deafness, showing Bezold triad and normal middle ears and eustachian tubes. On this basis, 57 cases were diagnosed as otosclerosis with stapes ankylosis, 7 as otosclerosis with nerve degeneration, making a total of 64 cases, or about 6 per cent of otosclerosis. In the latter group the patients had definite stapes ankylosis and developed a marked diminution of bone conduction during the years in which they were under observation. Of these 64 cases of otosclerosis, 47 per cent were males and 53 per cent females; there was a family history of deafness in 48 per cent; the deafness was bilateral in 94 per cent; tinnitus was a symptom in 76 per cent; paracusis Willisii, in 31 per cent; there was a diminution of the tickle reflex in 86 per cent; dizziness and vertigo in 4 per cent. Audiograms made in many of these cases were inconstant in character. In the series of 1,000 cases there were ninety-three cases diagnosed as nerve deafness; twelve of this group gave histories suggestive of otosclerosis. There were twenty-six cases of chronic catarrhal otitis media in this series which assumed many of the characteristics of otosclerosis. These patients at first showed signs and symptoms of eustachian closure, drum retraction and articular rigidity in varying degrees, and were treated by inflation and otomassage. Years later unusual permeability of the tube developed, with a dry scaly external auditory canal and a drum that was either slightly retracted or normal; in

some cases the skin of the auricle seemed to lose its normal firmness. These changes, in the observer's opinion, are due to a long continued congestion within the tympanum and ankylosis of the stapes, producing secondary atrophic changes in the petrous bone and its contents so that the adjacent nerves, especially the fifth, seventh, eighth and ninth, are affected. He does not, therefore, consider these cases to be true otosclerosis complicated by chronic catarrhal otitis media, but forms of the latter that have degenerated into a condition similar to otosclerosis. Chronic purulent otitis media can produce similar pathologic changes and symptoms; there were twenty-one such cases in the series that degenerated into a condition simulating otosclerosis. Such cases, in the observer's opinion, are to be considered as both pathologically and clinically distinct from true otosclerosis.

Modification of the hearing faculty through a change in position, in the presence of diplacusis, in a case of otosclerosis concerning a musician, was observed by Jellinek (1931), under employment of the Urbantschitsch harmonica. Aside from the patient's own observation that a single tone on this instrument was heard as two different tones by the two ears, this case presented the interesting feature that a change in position also caused a difference in the tone heard by the man, who sat upright and bent the body backwards, forwards, to the left and to the right. As he bent over to the left, he heard two different tones, apparently produced by the testing instrument, which was not the case. The musician was asked to sing the tones as he heard them, and an octave's difference was noted between the two vocal imitations. In the observer's experience, this phenomenon has never occurred before on a change of position, either in the partially deaf or in persons with normal hearing.

As a rule, otosclerosis occurs in individuals otherwise in enjoyment of perfect health—a fact rather contradictory to the metabolic-endocrinic assumption of its etiology—but the ear disease is sometimes complicated by other lesions of the auditory organ. In 45 of 126 cases diagnosed as otosclerosis, in the experience of E. P. Fowler (1933), a complicating nerve deafness was present, while 81 cases were not complicated by the same. A considerable number of cases showed no clinical evidence of past otitis media, and fully 50 per cent in cases with and without nerve deafness showed "past masked inflammation," i. e., definite signs of a past otitis media without a definite history of such an attack. The percentage of history of colds was high (62 to 80 per cent) in all cases without nerve deafness (with or without past otitis); but in the nerve deafness cases it was high only in uncomplicated cases (87

per cent) and in cases with a definite history of past suppuration (83 per cent). With all complications, the incidence of diseased tonsils and adenoids and their removal was high (69 to 91 per cent). Tinnitus was present in a large percentage of cases, especially in non-nerve deafness (82 to 88 per cent); in the nerve deafness cases there was no tinnitus in cases with a definite history of past suppuration. The existence of bilateral tinnitus in the absence of any other destructive lesion, by itself alone suggests otosclerosis, even in children (82 per cent of the cases). Vertigo was present in 13 per cent of the cases without nerve deafness and no complicating otitis, and in 28 per cent of those with past masked otitis. It was a symptom in the cases with nerve deafness in 20 to 38 per cent, respectively. Vertigo was not present in children or in a group of cases with a past history of otitis. Congestion of the membrana tympani varied from slight redness along the malleus to intense congestion in Shrapnell's membrane; it varied markedly between the two ears; it was found in a high percentage of ears in the nerve deafness cases (67 to 83 per cent); it was present in all children with past masked otitis, and in both ears in 81 per cent of these cases.

In pathologic studies of five cases of otosclerosis from Fowler's own collection, fourteen specimens from cases of otosclerosis presented by various foreign otologists and thirty-four from Johns Hopkins University, he found that all showed definite pathologic evidence of inflammatory processes in the middle ear, chiefly a thickened mucoperiosteum and often calcification of connective tissue. In some cases of otosclerosis, dense fibrous scar tissue extends from the middle ear cavity into the focus. In others there are fibrous adhesions between the otosclerotic focus and the anterior crus of the stapes, whether there is a bony ankylosis of the stapes or not. These findings indicate that otosclerosis may be present and not cause deafness, because causing no bony ankylosis of the stapes. All the deafness present in otosclerosis may not be due to bony ankylosis, even if present; some loss of hearing may be due to accompanying middle ear lesions. The finding of middle ear lesions does not preclude a diagnosis of otosclerosis (Fowler).

In a study of hearing by means of the audiograph, Yates (1928) was enabled to make a distinction between three different types of deafness: nerve deafness, otitis media with retracted membranes and adhesions; otosclerosis. The audiographs were found to show the characteristics of otosclerosis in cases of acute and subacute otitis media with recurrent attacks, suggesting that a chronic inflammatory middle ear process may eventually induce a pathologic condition

such as is encountered in otosclerosis. The claims of Fowler are confirmed and strongly supported by these findings.

A recent study by Bunch (1934), made possible by the Ball Fund, comes from the Oscar Johnson Institute, Department of Otolaryngology, Washington University Medical School, and contains numerous quotations from the literature collected in the first volume of "Otosclerosis" (1928). It is not presented as a complete study and the author admits that definite conclusions cannot be drawn. "It appears that a great deal concerning the nature of the progress of otosclerotic deafness can be learned by frequent tests and a careful study of the general physical condition of these patients."

Cunningham's paper (1934) entitled "Some Aspects of Otosclerosis," real before the Tennessee Academy of Ophthalmology and Otolaryngology, Chattanooga, is summarized by the author as follows: (1) In the light of our present knowledge, otosclerosis is probably a local manifestation of a general systemic dysfunction. (2) Heredity seems to have a certain definite bearing on this condition. (3) The fact that there are so many theroies as to the causation and so many methods of treatment plainly indicates that there is a great deal yet to be learned about this disease. (4) The otologist should be guarded in diagnosing this disease and should make an exhaustive study of a case before pronouncing it otosclerosis. (5) Present therapeutic measures seem unsatisfactory as to ultimate cure, but symptomatic treatment adds materially to the physical and mental welfare of the patient. The most hopeful prognosis belongs to those cases in which the disease develops late in life or the symptoms are of moderate grade. Such a case may be so gradual as to bring the patient to old age without disabling deafness.

In the resulting discussion, Anthony referred to the investigations carried out (1933) by Davenport, Milles and Frink, begun with a grant from the Otosclerosis Committee of the American Otological Society and completed in the Department of Genetics, Carnegie Institute of Washington.

As pointed out by Keen (1934), otologists are agreed that otosclerosis cannot be diagnosed with certainty during life. The diagnosis is still more difficult in children, because we do not have the help of certain additional signs, such as tinnitus and the type of onset of the deafness.

New Tests in Otosclerosis.—An "undulatory re-enforcement test" for hearing was devised by Gorinin (1931), in France, who utilizes a deep-tone tuning fork, which is placed against the mas-

toid process. On closing the auditory canal by pressing the tragus over it, the vibration of this fork sounds louder to a person with normal hearing when the pressure on the tragus is removed. By alternate pressure and release of the tragus the sound perception of the examined individual is respectively modified, making the test positive: 80 per cent of cases. No change in the intensity of the test nullifies it: 10 per cent; a diminished intensity makes a negative test: 10 per cent. While comparable to the Rinne test, its originator regards the new test as more sensitive, because in minor degrees of deafness of the conduction type the Rinne is positive, while the re-enforcement test is zero. His re-enforcement test also supplements the Weber test. In eight cases of otosclerosis the re-enforcement test was negative in both ears, except one instance in which it was positive on one side and negative on the other, worse ear. Gorinin points out that in otosclerosis the re-enforcement test becomes negative at the same time as the Gelle; it is not, however, a test of centripetal pressure, for the pressure in the Gelle test reduces hearing in the normal ear, whereas closing the auditory canal in the re-enforcemnt test increases the intensity of sound in the normal ear. Inversely, in otosclerosis the Gelle test does not modify the perception of the sound, but its intensity is reduced by the re-enforcement test. The intensity of the sound of the fork at the mastoid on closing the auditory canal by pressure on the tragus was found by Weill (1931), who studied the re-enforcement tests, to be diminished with great frequency in otosclerosis. This is apt to be the case when the centripetal pressure of the Gelle test does not modify the sound perception.

A new hearing test, designed especially to determine the presence of ankylosis between the stapes and the oval window, was proposed by Federici (1931), who utilizes either the La (96 d. v.) or the Ut (28 d. v.) fork. Having been put in vibration, the fork is placed against the mastoid and the time the patient hears the sound is noted in seconds. It is then placed against the tragus, which is pressed down lightly so as to close the external auditory canal. The time is noted, in seconds, of hearing the sound with the fork at the tragus after not hearing it at the mastoid. Federici's tests in persons with normal hearing showed that the sound with the fork at the tragus is heard about twenty seconds longer than with the fork at the mastoid. Tests with this method were made in forty-eight cases of otosclerosis, representing a typical form of stapes ankylosis. In all, the duration of hearing for the fork at the tragus was shortened; invariably the duration was less than ten seconds more than the hearing for the fork at the mastoid in one or both ears; in several cases

the hearing for the fork at the tragus was of shorter duration than the hearing for the fork at the mastoid.

Tests of hearing by bone conduction in a soundproof room and in the ordinary office room, University of California, were carried out by Knudsen and Jones (1931), who utilized the bone conduction receiver that has been developed for the audio-amplifier. In this instrument, which resembles an ordinary commercial telephone receiver, the circular diaphragm is replaced by a narrow strip of magnesium steel, placed directly across the poles of the receiver; an aluminum rod is attached to the center of this strip. The distal end of the aluminum rod is placed against the mastoid and the amplitude of vibration required barely to elicit the sensation of hearing is determined. By means of this method, the minimum threshold for bone conduction could be tested as high as 4,096 double vibrations, but precise measurements of the amplitude of vibration of the rod could not be made above 1,024 double vibrations. The acuity of hearing by bone conduction in normal individuals was found to be higher in the soundproof room than in the office room. In four cases of otosclerosis, with increased bone conduction as compared to normal persons, in the office room, the hearing by bone conduction in the soundproof room was normal or subnormal. In two of these cases the hearing was normal for frequencies up to 512 double vibrations and less than normal for higher frequencies; in two cases it was normal or nearly normal throughout the range of frequencies. These findings do not signify that increased bone conduction never exists, but that cases which "we have always associated with increased bone conduction do not show this increased bone conduction." From the diagnostic viewpoint, in the experience of the California investigators, charting loss in dbs hearing by bone conduction on the same chart with the air conduction, as suggested by Fowler (1933), is of definite advantage in diagnosis.

The audiographic studies of Yates (1928) have shown that the deafness of otosclerosis is of the uncompensated type, meaning that the patient does not hear the voice as well as his true degree of deafness, as indicated by the tuning fork tests, would permit him to hear. The reason is found in the "subsidence" deafness, in otosclerosis; the ends of words are not cut off clearly to the ear, but are drawn out, with the result that conversational speech, except at an extraordinarily slow rate, becomes unintelligible.

On experimenting with a new acoustic phenomenon described by Cigna, in 1930, to the effect that if a tuning fork is made to

vibrate in front of the ear and on cessation of sound perception the base of the fork is pressed against the tragus so as to close the ear, the sound is again perceived, Moulonguet and Doniol (1930) obtained varying results on testing normal individuals. In the majority of cases with apparently normal hearing the test proves negative with certain tuning forks, but is positive in over half of normal persons with the 435 tuning fork. In otosclerosis and other types of deafness, however, in which the bone conduction is increased, this test was found positive by the French observers with all three tuning forks (128, 435, 4,096). Absolute parallelism between positive results with the Cigna procedure and a negative Rinne was registered. This acoumetric method is not credited by them with any special value as compared to the customary hearing tests.

The use of the Western Electric Co. 1-A audiometer, which has a range from C to c8, for hearing tests, was found less satisfactory by Shambaugh (1930) for testing the lower tone range than the upper tone range. Testing with tuning forks gave him more satisfactory information than that obtainable by means of the audiometer, in the demonstration of defects in the lower tonal range. Five of his twelve illustrative cases were diagnosed as otosclerosis. The employment of an otoaudion with a telephonic instrument by which bone conduction can also be tested was reported by Sonntag (1930), who with this instrument constructed curves for air conduction as well as bone conduction in normal persons and in different types of deafness. Not much dissimilarity was shown between the curves of otosclerosis and severe catarrhal middle ear deafness. The curves of otosclerosis clearly indicate the prolongation of bone conduction, which is shown to be above normal. Some diminution for the very highest tones is found in most cases of otosclerosis, but the upper tone limit was but slightly reduced. Hearing by bone conduction was better than by air conduction for all tones that were heard. In otosclerosis with involvement of the auditory nerve Sonntag found the hearing for the upper tones reduced, both by air conduction and bone conduction, but the bone conduction was usually good for tones in the range of the speaking voice. The curve of bone conduction in these cases does not show a gradual but a sudden diminution: Thus, for tuning fork c4, bone conduction is almost normal, while for tuning fork g4 it is entirely absent.

A rapid method of making functional tests for office use was described and urgently recommended by Barkhorn (1930), who regards these tests as practically infallible. If in a case of chronic progressive deafness the tympanic membranes are normal and the eusta-

chian tubes patent, and the functional examination shows prolonged bone conduction, disproportionate loss of low tones with stapes fixation and a negative Rinne, the diagnosis of otosclerosis is evident.

An explanation of the Schwabach and Bing phenomena is contributed by Hallpike (1930). Of his sixteen cases of otosclerosis, eight showed a well-marked lengthening of the Schwabach test in an ordinary room, but no alteration in the absolute bone conduction. The findings in this series indicate that (although it may be present from the start, as in an illustrative case), cochlear involvement is merely a delayed process in otosclerosis. Involvement of the conducting mechanism in the oval window is constant and renders the cochlear involvement latent, at least in its early stage, so that the Schwabach test is approximately normal; the absolute bone conduction test indicates the extent of the cochlear involvement.

No case of otolsclerosis was found by Davis (1930) among 163 cases of deafness examined with the aid of audiometric and tuning fork tests. The observer defines otosclerosis as that type of deafness due to changes in the labyrinth capsule independent of the condition of the middle ear. Heredity and metabolic disorders appear to him as the most probable factor in the causation of otosclerosis.

Details concerning the vascular symptomatic test recommended by Nikolajew in Russia (1935), as simple and practical for diagnostic purposes, can be found under the heading of nonoperative treatment.

XIV. SURGICAL TREATMENT OF OTOSCLEROSIS AND OF TINNITUS.

The difficulties confronting the surgical treatment of otosclerosis through the establishment of a semicircular canal fistula are claimed to be partially overcome by the operative procedure of Sourdille (1930) in France, who had employed his method for several years before the publication of his technic. The Sourdille operation is based upon the improvement of otosclerotic deafness after opening the semicircular canal system. It consists in closing off the opened middle ear from the operatively created cavity of the mastoid portion, followed by temporary displacement of the tympanic membrane and interventions on the chain of auditory ossicles; next, opening the bony labyrinth by way of the horizontal semicircular canal, with subsequent closure of the fistula through a small thin flap devoid of periosteum. After the failure of surgery of the stapes and the insufficiency of exclusively labyrinthine surgery, his experience seemed to indicate that a favorable result is possible under the condition of acting simultaneously on the tympanic antrum and on the labyrinth. A new transmission apparatus is required for carrying the tympanic vibrations to the labyrinth; to provide this a permanent labyrinthine fistula must be established. After careful elaboration of a successful technic, beginning with a procedure in two stages, followed by a simplified method in a single stage, Sourdille finally decided upon a three-stage technic, the first two steps of which are destined for the transformation of the constituents of the tympanic antrum necessary to adapt them to the new mode of sound transmission. The third step accomplishes the establishment of the "decompressive" labyrinthine fistula, situated in equal parts on the semicircular canal and its ampulla; and at the same time the juxtaposition of the new tympanic apparatus with the labyrinth. If the tympanolabyrinthine junction is deficient all or part of the auditory improvement is lost; also, if the fistula becomes negative through the formation of a bony callus the improvement is not only lost, but the deafness continues to advance, as if the patient had not been operated upon. A definite outcome cannot be estimated before the end of at least two years. Sourdille at the time of the Madrid report (1932) had operated upon sixty-two ears with otosclerosis. His three oldest successful cases date back three years and remain unchanged. His last series of eight otosclerotics, operated upon by the three steps technic, include five good results, two moderate results, through adhesion of the flap between

the incus and the fistula, and only one temporary failure through rapid closure of the fistula by a bony callus. In his experience very good results are undoubtedly possible by means of the three steps technic, in a proportion of 75 to 80 per cent of the cases, provided the operator has a long experience with these procedures and that the patients are judiciously selected and encouraged to persist until the end of the treatment. These operations in his practice do not endanger life. More or less pronounced labyrinthine sequelæ occasionally follow, in the form of vertigo, aural tinnitus or disturbance of the muscular tonus, but these phenomena are rare and restricted to the very deaf, whose already altered labyrinth does not readily tolerate the decompression operation and contraction of scar tissue. The three steps technic is based upon the interpolation of an intermediate stage between the first and second step of the two steps operation. The purpose of the intermediary stage is to provide a thin epidermis flap from the auditory meatus for closing the labyrinth fistula. This contains cicatricial tissue free from periosteal elements and has therefore better sound transmitting properties. The third stage must be postponed until complete epidermization of the entire cavity has occurred, as well as a good union of the cicatricial mass with the tympanic membrane.

The great difficulty in Sourdille's operation, as seen by Moulonguet (1932), is the securing of a suitable graft to cover the artificial orifice in the wall of the labyrinth. In his modification of the Sourdille procedure a cutaneous flap is taken from the upper eyelid and this is fixed over the orifice made at the curve of the external semicircular canal. In two cases operated upon in this manner the thin graft was perfectly retained in place. The intervention dated back too short a time at the date of the report to permit a demonstration of the ultimate effect on the hearing faculty.

In discussing the surgical treatment of otosclerosis, Feldstein (1932) defined the Sourdille operation as a technically difficult procedure, based on too many obscure or uncertain points in our knowledge of the anatomy of the ear and the physiology of audition. In the opinion of Duerto (1930), the results of Sourdille's operation in two stages fully justify an optimistic attitude and point the way to a successful method. It is still open to technical improvements for control of the disease. Immediate results seem encouraging, and it remains for the future to show whether or not the remote results are proportionate to the risks involved.

A new technic was tried by Gunnar Holmgren (1931), in Sweden, in which antrotomy and removal of the incus is followed by the

detachment of a mucoperiosteum flap over the horizontal semicircular canal. This flap is turned down backwards and the endosteum is apposed with a suitable instrument to the semicircular canal. The permanent results of curettage with escape of fluid were unfortunately always very mediocre. Considerable technical difficulties arose in Holmgren's preceding attempts to obtain permanent results by selecting the anterior vertical semicircular canal and after trephining following detachment of the dura and replacing the dural flap over the denuded endosteum.

An important advance in the surgery of otosclerosis was seen by Berggren (1929) in the fabrication of an opening in the labyrinth at a point where it is not struck directly by sound waves, namely, beyond the circumferential outline of the tympanic membrane. The horizontal semicircular canal was selected by him for this intervention as the most accessible for entering the capsule outside the middle ear. The permanent success of the operation depends upon the prevention of secondary closure of the new bony orifice. This objective was aimed at in a case of otosclerosis by making an orifice in the horizontal semicircular canal and keeping the orifice open by means of wax which was pressed into the margins of the defect. The formation of granulations was apparently prevented by the wax and a yielding portion of the labyrinth wall persisted. The procedure was adopted in the case of a woman, thirty-nine years of age, who had been unsuccessfully treated for otosclerosis by means of intravenous calcium therapy and injections of parathyroid hormone. The immediate as well as the remote surgical result was good beyond expectation, as the patient, previously deaf for practical purposes, after the operation was actually able to understand spoken words with the operated left ear. The improvement persisted for the half year she could be kept under observation, and the aural tinnitus was diminished. In this paradoxical case of otosclerosis, with an additional secondary atrophic degeneration of the membranous labyrinth, the prospects of benefit through operative intervention with removal of the mechanical obstacle in the labyrinth capsule were very slight; but the favorable outcome shows that even such complicated cases may be benefited.

In a manner similar to that of Sourdille, Jenkins (1913) had previously operated and always with immediate improvement of hearing, which vanished within six months. The aural tinnitus in all his cases disappeared and did not return even with aggravation of the deafness. The external semicircular canal was opened by him in a later and desperate case of otosclerosis with tinnitus and complicated by ostitis

deformans; the tinnitus at once subsided. His older experiences were reported at the International Congress of Medicine in 1913.

The following procedure, so far tried only on the cadaver, is recommended by Wittmaack (1933), whose proposed operative treatment of otosclerosis is based on his stasis theory and aims at diminishing or removing the venous stasis, the assumed cause of the otosclerotic changes. Two veins enter into consideration for the drainage of the blood from the otosclerotic focus, one of these veins accompanying the major superficial nerve, while the other passes more or less by itself. Both veins communicate with a wide venous plexus, normally well filled with blood. In the presence of otosclerosis these veins, whether communicating with the venous plexus of the middle meningeal artery or with the carotid plexus or both, are found to be very strongly distended. According to Wittmaack's assumption, occasional congestive states due to regional anatomic peculiarities may become permanent in predisposed cases, with the result that a retrograde blood current towards the otosclerotic focus becomes established. His counteracting operation consists in the division of these veins close to their emergence from the cranial cavity. A trephine orifice is made in the temporal region and the dura is raised, exposing the middle meningeal artery and the veins that are to be divided. The procedure might be given a trial, Wittmaack thinks, in not too far advanced cases of otosclerosis.

Paracentesis, in the form of a crescentic incision in the tympanic membrane, between the inferior-anterior margin and the umbo, was performed by Dundas Grant (1933) in a case of otosclerosis; the artificial perforation remained open for three-quarters of a year.

A report on the first twenty operated cases of otosclerosis came in 1934 from the Nose, Throat and Ear Clinic of the University of Hamburg, Germany. The author, Heinz Rollin, states that the operation performed in these cases was the so-called dura ventilation over the tegmen tympani (Wittmaack), which aims at preventing a retrograde venous blood current by way of the carotid plexus or from the middle meningeal plexus into the bone of the labyrinth capsule. This objective is accomplished through the division of the veins which penetrate with the major superficial nerve through the tegmen tympani. All that is expected from the operative intervention is an arrest of the still progressive process, rather than an improvement of the hearing. In the Hamburg Clinic the operation was performed under ether anesthesia, required three-quarters of an hour and was readily tolerated by all patients. The surgical wound always healed

by first intention. After careful consideration of all factors here concerned, Rollin feels justified in the statement that the advance of the pathologic process was stopped in 90 per cent of the cases. The partial subsidence or entire disappearance of the tinnitus is accomplished in a high percentage of the cases. The most suitable are incipient cases which show a distinctly progressive character. Far advanced deafness is a counter-indication, as the procedure merely aims at the prevention of further aggravation.

Nesfield (1931), in England, described an operation performed by him in numerous cases of otosclerosis, primarily designed for the relief of deafness due to blocking of the eustachian tube. The purpose of the intervention is to open an air passage into the middle ear and also to drain it. It is claimed by Nesfield that this intervention "opens the eustachian tubes, improves the mucous membrane of the tympanum, relieves pressure in the cochlea and brings about an absorption of exostoses, adhesions and new bone, and relieves the auditory nerve." His own surgical material included a number of cases of otosclerosis. In no instance was the deafness aggravated by the intervention. As a rule, the hearing was definitely improved; in other cases, without definite improvement, the hardness of hearing did not progress. In a few instances the improvement persisted as long as five years at the time of the report.

Aural Tinnitus.—The historical-critical essay of Moulonguet (1934) on the surgical treatment of aural tinnitus is of interest in this connection. A distinction is made by him between objective and subjective ear noises, and the former are again subdivided into ear noises of vascular and muscular origin. The control of vascular noises was attempted especially by means of ligature of the internal carotid artery, with only moderate results, the effect being positive in at most one-third of the cases described in the literature. With variable success, ligature of the external carotid and the vertebral artery have likewise been performed with the same objective. Surgical intervention has likewise proved unpromising for the control of muscular ear noises, because of the difficulty of identifying the responsible muscle in a given case. Subjective ear noises must be managed according to their site of origin. So-called reflexogenic bruits may disappear after interventions in the domains of the trigeminus and the vagus nerve; for example, after dental operations, resection of the nasal septum, or interventions on the gastro-intestinal tract. Ear noises of middle ear origin are tentatively treated by interventions on the tympanic membrane and the auditory ossicles; noises originating in the internal ear, by interventions on the labyrinth, puncture of the round

window, opening the round and oval window, opening the labyrinth, the saccus endolymphaticus; or interventions on the meninges (lumbar or suboccipital puncture, or incision of the dura), division of the acoustic nerve; or periarterial sympathectomy according to Leriche. All the enumerated methods of treatment, however, cannot guarantee a cure of tinnitus at the present state of our knowledge, and surgical interference must still be reserved for a few exceptional cases.

XV. TREATMENT, NONOPERATIVE.

The treatment of otosclerosis, as pointed out by J. Gordon Wilson, in 1932, is very disappointing. Maintenance of the general health is essential; detection and treatment of septic foci is of the greatest importance. Marriage and childbearing should be discouraged for otosclerotic women, not only because of their bad effect on the patient, but also because of the probable transmission of the disease to the offspring. The occasional observation that an acute attack of otitis media arrests the course of otosclerosis, suggests a possible therapeutic measure in the form of an artificially induced middle ear inflammation. Various irritants have been tried for this purpose, but Wilson prefers the use of radium, in sufficient amounts to cause "a sharp reaction." Good results are sometimes achieved, but the treatment is unreliable.

Upon the basis of observations and investigations conducted in the Oto-Rhino-Laryngological Clinic of the University of Catania, Carco (1934) points out, in connection with five new cases, that the fundamental rule in the treatment of otosclerosis must consist essentially in surprising the disease, as it were, in the phase of presclerosis described by Citelli (1913, 1914). This stage in all probability often, if not invariably, *precedes otosclerosis*. It is characterized by a plastic infiltrate which immobilizes the stapes or limits its movements and acts on part of the labyrinth. By means of timely iodine medication, much of this infiltrate is claimed to have disappeared in Citelli's patients (children and adolescents), whereas without its use the plastic infiltrate progressed to the stage of a more or less intractable osseous dystrophy. The recognition of the presclerosis stage is of the greatest practical importance, on account of its amenability to iodine and iodo-calcium therapy.

Improvement of otosclerosis was noted by Birkholz (1930, 1934), after intravenous treatment with calcium bromatum, which not only relieved the aural tinnitus, but was followed also by better hearing, with increased distance for the voice as well as in tuning fork tests. The favorable effect is referred by the observer to the stimulating action of the calcium on the imperfectly developed mesenchymal tissue in these cases.

An attempt was made by Loewenstein (1934) to ascertain if the blood calcium content in man may be raised by bone transplantation. In eleven verified cases of otosclerosis, a heterogeneous bone

transplantation was applied under the subcutaneous cellular tissue of the anterior thoracic wall. The blood calcium content was not increased thereby and no modification of the otosclerosis, objective or subjective, could be demonstrated.

The local application of thyroxine is recommended in the treatment of otosclerosis and similar types of deafness, by Albert A. Gray (1935), whose investigation was carried out at the Ferrens Institute, Middlesex Hospital, England. This treatment—the rational sequence of its originator's vasomotor explanation of otosclerosis—consists in the local application of the remedy to the ear, aiming at the correction of the deficient vasomotor response in the small blood vessels of the ear through the production of an active regional congestion without inflammatory reaction. Fourteen otosclerotic patients were treated and very considerable improvement was obtained in seven of this number (50 per cent). Tinnitus when present was greatly relieved. Wax also began to be secreted again. The subjective symptom of paracusis, usually considered of very unfavorable augury, is no contraindication to this method of treatment, for paracusis was present in two of the most successful cases. Unsuitable for this treatment are very advanced cases in the last stages of the disease and those in whom there is a serious loss of bone conduction or conditions in which the loss of hearing for high tones is very marked. In summarizing, Gray says that a large proportion, about one-half of the cases of otosclerosis and dry middle ear catarrh can be greatly improved in regard to better hearing and tinnitus by the intratympanic injection of thyroxine. The technic of the procedure is very simple for an expert otologist. Thyroxine in the form of a fine powder suspended in four minims of distilled water is injected through the tympanic membrane into the inner middle ear, by means of an ordinary good hypodermic syringe with a rather long small caliber needle. The treatment is almost or entirely painless and does not interfere with the patient's daily activities. The action of thyroxine persists for a long period of time; it is not yet possible to say how often the treatment may have to be repeated. Improvement, when it occurs, lasts in some cases for several weeks, but sooner or later the effects must be expected to pass off.

Injections of parathyroid extract served to improve the hearing and diminish the tinnitus, in the experience of Watson-Williams (1929) in some typical cases of otosclerosis. When the therapeutic effect apparently wore off after a few months small doses of calcium glycero-phosphate proved useful. It goes without saying that in the treatment of otosclerosis it is more important to improve the hearing

for ordinary conversation than for tuning forks or acoumetric instruments.

Pancreatic extract was administered by Gottlieb (1932) in seven cases of otosclerosis, with some auditory improvement in most of the treated patients; but the period of observation was too short at the time of the report to permit any definite conclusions as to the efficacy of this particular medication. Moreover, temporary fluctuations in the hearing capacity are not uncommon in otosclerosis.

Adrenalin medication, in the form of small subcutaneous doses of the drug, combined with administration of calcium and cod liver oil and very small oral doses of vigantol, is advocated by Rosenfeld (1933) as a valuable treatment of otosclerosis. In early cases this treatment has never failed to induce definite improvement, in his experience. Bobone, in Italy, in 1934, confirmed the favorable results of adrenalin treatment obtained by him twenty years ago (in 1914), and expressed his satisfaction with the analogous experience of Rosenfeld.

Three typical cases of otosclerosis, two in men and one in a woman, were treated by Mirvish (1930) with a parathyroid preparation (parathormone Lilly), on the basis of the assumption that the causative low concentration of blood calcium may be the result of hypoparathyroidism. The remarkable improvement in the hearing of these patients was "a distinct surprise" to the observer, who had not ventured to hope for more than an arrest of the progressive deafness. Otosclerosis, among other conditions, is considered by B. L. Bryant (1932) as associated with signs of hypothyroidism and sometimes benefited by judicious administration of thyroid extract.

Arsenic medication, oral or subcutaneous, had a favorable effect in otosclerotic (54 out of 88 cases) as well as other types of deafness in an experience, extending over four years, of Wodak (1929). Good results were reported by Noack (1929) from the use of a proprietary preparation.

In the local treatment of otosclerosis, Woods (1929) has made use of iodin and radium. The former was found to yield better results in the earlier cases, while radium proved helpful in those of prolonged standing. Improvement is claimed to have been achieved and maintained in some of the treated cases.

Kahan (1934), on the basis of experience in the Kiew Medical Institute, attempted to modify otosclerosis by means of vitamin medication and apparently obtained some improvement in certain

cases. In order to determine the therapeutic value of various substances with vitamin contents, the otosclerotic patients of the Clinic for Diseases of the Ear, Throat and Nose were divided into six groups, according to the prescription of one or the other product. The first group received only dry yeast. The second group received codliver oil. The third group received dry yeast and general treatment with the Bach quartz lamp. (The human dermis contains a large quantity of inactive vitamins "d," for the incorporation of which in the active form they must be subjected to the action of the ultra-violet rays. Through the simultaneous administration of dry yeast the inactive vitamin d in the dermis is replaced; furthermore, vitamin b, which is always an active vitamin, is supplied to the organism.) The same considerations apply to the fourth group, which received only yeast subjected to the action of the ultra-violet rays, without treatment with the quartz lamp. The fifth group received yeast subjected to the action of the ultra-violet rays and furthermore mud applications around the neck on alternate days, six to twelve sessions. The sixth or complex therapeutic group received a combined treatment with cervical mud applications, exposure of the entire body to the action of the quartz lamp and simple yeast. Repeated blood examinations at the beginning and in the course of the treatment showed a slight eosinophilia in about 15 per cent of the otosclerotic patients. No specific result was demonstrable after three months from the use of dry yeast and the exclusive employment of cod liver oil. (First and second groups.) Of the third group, nine of seventeen patients subjectively experienced a decrease of the tinnitus (60 to 70 per cent) and better hearing. The fourth group was more obviously benefited, but only for a short time; the old phenomena recurred from ten to fourteen days after the treatment, also after repeated courses of the same. Four patients of the fifth group showed the best result during a month and a half at the end of the treatment. Eight patients returned, complaining of renewed aural tinnitus and recurrent loss of hearing.

The sixth group (combined treatment) gave the best results, for ten of sixteen patients are free from tinnitus since a month after the treatment, and in five others, in whom the irradiation had been somewhat modified, the outcome was satisfactory to the patients. The observer concludes that further study of the conditions and indications for the employment of yeast subjected to the action of ultra-violet rays; the Bach quartz lamp; Rusian mud treatment; separately or in various combinations, must be recognized as highly desirable for otolaryngologists, for only a collective inquiry can elucidate a question so full of interest as that of the treatment of otosclerosis.

Roentgen Ray and Radium Treatment of Otosclerosis.—There is as yet no consensus of opinion as to the mode of action of these rays on the otosclerotic process. A number of reports on x-ray and radium treatment of otosclerosis, for the most part in the form of local irradiation of the region of the ear, were reviewed and discussed by Desjardins (1931) in this country. In some of the cases the regional treatment was combined with irradiation of various internally secreting glands (parathyroid, thyroid, pituitary). The conclusions arrived at by Desjardins are quoted verbatim in the following: "It is difficult to understand how a disease such as this can be influenced to any great extent by roentgen or radium rays. The evidence furnished by some of the foregoing reports is not substantial and some of it is worthless. Moreover, the assumption of an inter-relationship between otosclerosis and certain hypothetical disturbances of the pituitary and parathyroid glands cannot be said to have much foundation. Many of the cases of otosclerosis in which improvement in symptoms was reported to have followed roentgen ray or radium treatment must, therefore, be excluded. Especially is this true with reference to hearing, because the impression or opinion of the patient is notoriously prone to be affected by suggestion. This is a field of therapeutics in which *post hoc propter hoc* deductions have been legion. Having made these ample reservations, there remains, nevertheless, a certain proportion of patients who appear to have been unquestionably benefited. It is noteworthy also that the tinnitus seems to have been influenced more than the impairment of hearing. . . . It is probable that the cases in which radiotherapy is followed by improvement are those in which the disease is associated with chronic inflammatory changes and a measure of leucocytic infiltration. This would explain the improvement."

Roentgen irradiation is recommended by Rejto (1934, in Hungary, as a therapeutic measure. Otosclerosis has not so far received much attention in his native country. He deplores the costliness of modern American hearing appliances which favorably utilize the existing bone conduction in these cases.

Otodiathermy.—Numerous observations of Last (1929) have shown that properly conducted diathermy treatment is capable of relieving and sometimes more or less durably removing otherwise intractable symptoms. In several cases also the hearing of the patient seemed to be considerably improved after the treatment, although otodiathermy aims in the first place at the removal of the other subjective disturbances. General diathermy of the entire body is recommended as inducing arterial dilatation and better circulation, with an

improved blood supply of special organs. The ear electrode devised by Last serves for the local treatment of the ear.

Diathermy treatment, with utilization of heavy foil electrodes, was employed by Guttmann and Kulvin (1931) in eleven cases of otosclerosis with bilateral deafness and aural tinnitus. The current was regulated according to the patient's subjective sensations and rarely exceeded 400 to 500 milliamperes. The hearing was tested at weekly intervals under standardized conditions. Nine of the eleven patients were subjectively improved after treatment, but the hearing tests failed to show any improvement. The remaining two patients felt no benefit and the negative result was confirmed by the tests. The tinnitus was variably modified, apparently benefited in four cases, unchanged in two cases, and aggravated in five cases. Judging from this small material, it cannot be denied that diathermy has little or no effect upon the hearing and ear noises in otosclerosis.

The ultimate success of otodiathermy treatment in otosclerosis, in the opinion of Schaefer (1932), in Germany, must depend upon the degree of advance of the pathologic process in the labyrinth capsule. The chief value of this conservative procedure is to increase the circulation in the middle and internal ear, eventually also the mobility of the ossicles, in the earlier cases. Otodiathermy must be supplemented by other methods of treatment: locally, simple and sinusoidal faradization, besides general medical treatment according to indications in a given case. While the tinnitus can be relieved sometimes, Schaefer regards it as doubtful if the hearing is definitely improved by otodiathermy. In two of four treated cases of otosclerosis the tinnitus was relieved and the hearing was improved, as shown by voice tests. No improvement was obtained in one instance, in spite of long-continued treatment. The fourth case was temporarily benefited, but a definite effect of the diathermy treatment appeared doubtful.

Five women suffering from otosclerotic deafness were treated with diathermy by Moulonguet and Doniol (1930), in France, who utilized an active electrode introduced into the external auditory canal, but none of these cases showed any improvement of hearing under or after the diathermy treatment. On the other hand, diathermy was employed by Deliencourt (1930) in three cases of otosclerosis, in all of which the hearing was improved and the ear noises were relieved. Diathermy, without too great elevation of temperature, was recommended in otosclerosis by Lasagna (1932).

In discussing the indications for the high frequency current in the treatment of deafness, Mayoux (1932) points out the vasodilatation resulting from its use in the form of diathermy. In his opinion, seeing that vasodilatation is one of the chief anatomic characteristics of otosclerosis, diathermy is considered by him as definitely contraindicated in these circumstances.

No benefit from diathermy in otosclerosis was observed by Hollender (1930), in whose experience the symptoms may actually become exaggerated.

The favorable outcome of treatment with high frequency currents in the experience of some observers, in otosclerosis and other forms of deafness, is referred by Ramadier, Chaussé and Bzowski (1930) to a purely temporary functional improvement due to circulatory alterations in the labyrinth. It is only in the absence of organic lesions that the high frequency current is effective.

The *electro-phonoid* method of treatment of otosclerosis, its results and its technic are described in Otosclerosis, Value 2. It is defined by Yearsley (1932) as a method of local treatment; it is a form of ear massage, but a massage by sound, not by instruments, and is the normal physiologic stimulus for the organ of hearing. This method was utilized by him in thirteen cases of otosclerosis, all associated with chronic auto-intoxication of intestinal origin, so that both conditions required and received treatment. Very definite improvement followed in ten cases, slight improvement in two cases, while only one patient was not benefited. In order to secure the best results, Yearsley recommends a combination of electrophonoid and intestinal treatment. The electrophonoid treatment alone was employed by Cathcart (1929) in 172 cases of chronic deafness, diagnosed as otosclerosis; ninety of this number were definitely improved by these means. In his later experience, 115 of 213 cases showed definite improvement. The electrophonoid method proved highly beneficial in the experience of Pruvost (1933) in two cases of otosclerosis, both of long standing, associated with progressive deafness, aggravated in one instance by childbearing. By a series of fifty treatments the patients' hearing was markedly improved, as measured by the hearing distance for both whispered and ordinary speech. Still further improvement and maintenance of the gain, respectively, could be noted in these cases two months after the treatment had been discontinued.

The treatment of various forms of chronic deafness, including otosclerosis, by means of ionization with zinc sulphide or with sodium

silicate applied with the negative pole, diathermy and the use of the Zund-Burguet apparatus, for re-education of the hearing, proved beneficial in the experience of Neville (1929): Diathermy and electrophonoid treatment led to seeming definite improvement of the hearing in an illustrative case of otosclerosis.

Electric ionization with employment of a 2 per cent sodium iodide solution was given a trial in otosclerosis therapy by Malherbe (1928), in France, often with satisfactory results in the form of improved hearing, when applied in the earlier stages prior to the development of the terminal sclerosis. The high frequency current, both in the form of diathermy and of effluve, with a specially adapted ear electrode, was utilized in various forms of deafness, including otosclerosis, by Caboche and Oumikowa (1929); some benefit was apparently obtained

About seven years ago the utilization of "sound waves" with frequencies lying above the human limit of hearing, therefore inaudible, was proposed by Mulwert and Voss (1928) in the treatment of chronic hardness of hearing, not excepting otosclerosis. The treatment must be kept up for at least four weeks, usually longer. Ultra-high frequency sound waves were utilized by Voss in eight cases diagnosed as typical bilateral otosclerosis, which were definitely improved with respect to the tinnitus as well as the hardness of hearing; shown by tests with the whispered as well as the ordinary speaking voice. The best results were obtained in youthful patients or in cases where the deafness was not of long standing. The effect of the ultra-high frequency sound waves is attributed by Voss to their electrochemical action on the auditory nerve; this action, as indicated by his tests, resembling that of the galvanic electric current. The experience of Hamm (1930) with this method at first proved disappointing, but finally better results were obtained by a slight modification of the procedure.

In some selected cases of chronic deafness, ultra-high frequency sound waves were given a trial, with inconclusive results, by Frenzel and Scheiff (1932). Of four reported cases of otosclerosis, two showed improved hearing for the whispered or spoken voice; two showed no improvement. This mode of treatment is regarded by them as still in the experimental stage. Ultra-high frequency, produced by an electromagnetic apparatus, was utilized by Kopilowitsch and Zuckermann (1932) in the treatment of various forms of deafness, including five cases diagnosed as otosclerosis. Here the rather complicated treatment resulted in merely very slight and only temporary improve-

ment, or proved altogether inefficient. The employment of high frequency sound waves proved beneficial in Reuter's (1932) experience in two cases of otosclerosis, both showing improvement in hearing after treatment.

The therapeutic influence of short sound waves (ultra-high frequency sound waves) on the ear and the different methods of their production and clinical application were reviewed by Perwitzschky (1933), who finds that ultra-high frequency sound waves up to 1800 Hertz frequencies can be compared in intensity with the sound waves of a Galton whistle. Only one of forty-six treated cases of otosclerosis showed definite improvement; twenty cases showed doubtful improvement and in eleven of these last cases the aural tinnitus was partially or completely relieved.

Electric hearing devices, of telephone type or constructed on the principle of the modified Bárány apparatus have been suggested for further increasing the bone conduction of otosclerotic patients and relieving tinnitus. A physiotherapeutic method, including local treatment with diathermy followed by the application of galvanism and then of the slow surging current to each ear separately, was reported by Thornburg (1931), who concluded that "otosclerosis" cannot be helped by this method."

Various forms of electricity, including the ultra-violet ray, were applied by Mounier-Kuhn and Ceccaldi in France (1932) in the treatment of chronic deafness. Of nine cases of otosclerosis, six were treated by ionization; sodium silicate was used in all cases, plus potassium iodide in two instances. The distressing tinnitus was remarkably relieved in all patients, and one of the number showed a definite improvement in hearing. In four cases the hearing was slightly improved; no auditory improvement followed in one instance. The tinnitus was most efficiently relieved in the two cases of combined ionization; the hearing was here but slightly improved. One case of otosclerosis was treated unsuccessfully with diathermy. Treatment with ultra-violet rays for relief of tinnitus in two patients proved of only moderate benefit.

In a "Communication" to the Second International Otorhinolaryngological Congress (Madrid, 1932), Wicart discussed the treatment of deafness caused by tubal obstruction with subsequent otosclerosis, pointing out that treatment aiming only at the middle ear lesions can be of little use until the pneumatic function and tubal permeability have been restored.

In view of the known influence of pressure on the common carotid artery upon subjective auditory sensations, this pressure, applied for five to seven seconds over the thyroid cartilage, was investigated by Nikolajew (1935), in Russia, with the following results: In diseases of the middle ear (obstacle to sound conduction), the ear noises cease completely during the pressure, reappearing on removal of the finger. In the presence of an affection of the acoustic nerve (obstacle in the sound-perceiving apparatus), the pressure exerts no influence upon the subjective auditory sensations. In the presence of spontaneous nystagmus the ear noises and also the nystagmus cease at once on pressure upon the carotid artery. In the case of middle ear disease the phenomenon is referred to changes in labyrinth pressure. When the cochlear nerve or Corti's organ are affected, pressure upon the carotid artery naturally cannot modify the ear noises. The influence of carotid compression upon the vestibular apparatus is not so marked.

The following statement, of historical interest, is found in Parry's Aphorisms, quoted by Wm. Harvey (1855), over eighty years ago: "When the rushing sound is waving or alternate, as it usually is, each rush is exactly synchronous with systole of the heart; and when the disorder has been more or less constant, and has affected one early only, I have often been able, pro tempore, entirely to remove it and always to alleviate it, by compressing the carotid artery on that side."

In about eighty patients with aural tinnitus of nervous origin, Bárány (1935) applied submucous or intravenous injections of local anesthetics. In a number of cases the tinnitus essentially diminished or even disappeared entirely soon after the injection. On employment of novocain the effect lasted twenty minutes to one hour, and up to eighteen hours with percain. The favorable reaction was noted in the cases with continuous (not pulsating) tinnitus, and the effect recurred on repetition of the injection. Even on daily repetition of these anesthetic injections no injurious sequelæ were observed.

Syphilis, congenital or acquired, has been practically eliminated as a possible factor in the etiology of otosclerosis, on the basis of the data collected by those investigators who have given their attention to this phase of the subject. Favre (1932) raises the question if a syphilitic otosclerosis is admissable and surmises that in a few exceptional cases otosclerotic bone changes in the labyrinth capsule may be of specific origin. Evidence of syphilis was found by him in at most 5 per cent of the cases of otosclerosis. Among 390 otosclerotic pa-

tients seen in Escat's (1930) practice since 1908, syphilis, either congenital or acquired, could enter into consideration as a probable etiologic factor in only fifteen cases and was verified, by the Wassermann test or ex juvantibus, in only four instances. It is only exceptionally and in combined cases that antisyphilitic treatment is indicated or even advisable. According to Escat's (1931) experience, it is generally useless and may prove actually injurious. The diagnosis of otosclerosis developing on a soil of congenital syphilis was rendered by Bernard Lapommeray (1933) in the case of a boy fourteen years of age, with a positive Wassermann reaction, whose loss of hearing had progressively increased in the last five years. The onset of otosclerosis was unusually early in this case and in the observer's opinion was hastened by the syphilitic infection. Antisyphilitic medication in otosclerotic patients was rejected by Favre (1932) on the basis of experience in Escat's clinic. In the pathogenesis of otosclerosis, Riccitelli and Franchini (1932) take into consideration the embryologic factor, on account of the presence of remnants of embryonic cartilage in definite zones, endocrinic anomalies, and the influence of a chronic infection, such as syphilis. The last named factor is surmised to explain the second factor, and both, in the opinion of the authors, are necessary for the activation of the first factor.

Clinical Notes.

X.

BILATERAL PARALYSIS OF THE LARYNGEAL ABDUCTORS OF INFLUENZAL ORIGIN.*

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When a patient, giving a history of syphilis thirteen years ago, consults you regarding a bilateral paralysis of the posterior crico-arytenoid muscles, it is logical to think of a bulbar lesion. Before committing ourselves to a diagnosis we must, however, exclude any other cause of the paralysis. Last fall, in my service at the Notre Dame Hospital, I saw such a case which later required a tracheotomy to prevent suffocation. But laboratory and neurologic findings definitely eliminated syphilis. The history of the patient is as follows:

REPORT OF A CASE.

Case 1.—G. A., male, aged 43 years, came to the dispensary of the hospital November 16, 1934, on account of difficulty in breathing.

On examination we found a bilateral paralysis of the vocal cords, which were in a paramedian position. There was no atrophy, but during the effort of inspiration the cords were drawn downward toward the trachea. On phonation they came slightly together. The glottis was narrowed, and the patient breathed with difficulty. There was hyperemia of the mucous membrane of the larynx, without ulceration or edema. Sensibility was normal. The voice was hoarse. There was no lesion of the epiglottis or hypopharynx. There was a chronic cryptic tonsillitis. Sensation and movements of the soft palate were normal.

There was a traumatic deviation of the nasal septum to the right, with a slight external twisting of the nose to the left.

*Read before the Congrès français d'Oto-Rhino-Laryngologie, Paris, 16 Oct., 1935.

The cervical and submaxillary glands, as well as the thyroid gland, were not hypertrophied.

The patient denied any previous throat trouble. At the age of thirteen years he had typhoid fever, and about the same time pneumonia. These two affections confined him to the hospital for nine months. The patient contracted syphilis at the age of thirty years, for which he was treated very energetically at that time. On September 18, 1934, he had a very severe attack of influenza, and fifteen days later he noticed a slight hoarseness, accompanied with some difficulty in breathing. Almost one month later, on October 12th, the patient suffered from recurrence of the influenza, which caused an increase of the laryngeal trouble. From this time on, respiration became more and more labored, and one month later the patient entered the hospital.

X-ray examination of the chest excluded any enlargement of the tracheobronchial glands, mediastinal tumors or dilatation of the blood vessels.

In order to prevent asphyxia, tracheotomy was performed the same day by my assistant, Dr. J. Brault. Postoperative sequelæ were normal, and two weeks later the examination was continued.

There was no Argyll-Robertson pupil and accommodation was normal. No lesion of the eyes, and vision was excellent.

The Wassermann reaction of the blood and of the cerebrospinal fluid was negative.

The patient had never suffered from diphtheria, lead poisoning, malaria, disseminated sclerosis or tuberculosis.

He smokes moderately, and does not use any alcohol.

There was no history of any injury to the neck.

A careful and minute neurologic examination, by Dr. Jean Saucier, showed a normal condition of the brain and spinal cord. Indeed, there was no involvement of the central nervous system. The bulbar and spinal nuclei, as well as those of the neighboring cranial nerves, were not affected. Furthermore the pyramidal tracts were intact. There was no appreciable trouble of sensation, a fact which in consequence eliminates the syringomyelia. All reflexes were normal.

As the patient did not manifest any neurosyphilitic stigma, it was not judged necessary to give him a provocative dose to be followed by another Wassermann.

Strychnine was prescribed.

The posticus paralysis persisted without any change for one month after tracheotomy. Then, at the end of the fifth week, a slight abduction of the left vocal cord was noticed. Abduction of the right cord appeared some time later. Adduction was normal. Improvement continued gradually, and at the end of December we began to block off the tracheotomy cannula, from time to time, in order to allow breathing through the larynx. On January 21, 1935, the tracheal wound was closed by means of deep sutures, and healing was obtained by first intention.

Desirous of completing the therapy by physical agents, Dr. Laquerrière was asked to take charge of the patient. Infra-red rays of thirty minutes' duration, directed over the anterior part of the neck, were then administered. This combined treatment had a very good effect, for the paralysis diminished. Breathing was excellent and the voice became clearer. At the end of April the left vocal cord so far recovered that the intermediary position was maintained, while abduction of the right cord, though still limited, was now more apparent. As the prognosis of paralysis of the laryngeal dilators, due to infective neuritis of the recurrent laryngeal nerves, or any other cause, is rather unfavorable, it will be interesting to follow this patient's further course, in order to see if complete recovery will occur.

Now let us consider the etiologic factors that could possibly produce a paralysis similar to the one from which our patient suffered. First, and as always in such cases, comes syphilis. However, the specific infection dated back thirteen years, and at that time he had been treated in a very thorough and satisfactory manner. At the onset of the paralysis of the posterior crico-arytenoid muscles both the Wassermann and the cerebrospinal reactions were negative. A most minute neurologic examination showed the complete absence of any stigma of neurosyphilis. And nine weeks after the tracheotomy, without any specific treatment, which had not been judged necessary, the cannula was removed. Since then, with the use of strychnin and physical agents, the improvement continued. It is also probable had syphilis been the cause of the paralysis this patient would still be wearing the tracheotomy tube, and perhaps would require it for many years to come. In spite of the great admiration that I have for my late teacher, Lermoyez, and many of his school, I am still of the opinion that all abductor paralyses of the larynx are not due to syphilis.

I would like to again emphasize the fact that the x-rays showed the mediastinum free of any lesion. The esophagus was normal. The patient never had neck injuries, operations, tumors or enlarged glands.

Needless to consider the syndrome of the posterior jugular foramen, or the more complex syndrome of the associated laryngeal paralysis, for the movements of the soft palate, tongue, shoulder and sterno-cleido-mastoid muscles were normal.

We can eliminate toxic neuritis, because the patient lived an outdoor life, took neither alcohol nor drugs, and smoked moderately.

Arthritis of the crico-arytenoid joints was excluded for the reason that on my first examination there was no manifestation of an acute laryngitis, and one could hardly imagine such a condition developing in a chronic manner.

As a last resort, we have then to consider infective neuritis of the recurrent nerves. If we review the history of this case we see that before the 18th of September, the health of the patient was excellent. However, on this date he was seized with a severe attack of influenza, and two weeks later a slight difficulty in breathing began to appear. On the 12th of October, a recurrence of the influenza so aggravated the laryngeal trouble that a tracheotomy had to be performed on the 16th of November. On the 21st of January, the tracheotomy tube was removed. Since then respiration has been good. After excluding all other possible causes of this condition one is driven to conclude that this paralysis of the abductors of the glottis resulted from an infective neuritis of the recurrent laryngeal nerves of influenzal origin. Furthermore, we know that cases of infective neuritis of the recurrent nerves are met with from time to time, an example of which I published in 1929. This was a case of a young man with a negative Wassermann, who suffered from a paralysis of the posterior crico-arytenoid muscles secondary to typhoid fever.

At the beginning of July, bilateral abduction was slightly more pronounced and adduction was normal. The voice had been clear for two months previously, and breathing was perfectly free, even during moderate exertion.

I do not have to consider here the value of the Semon-Rosenbach's law, now abandoned by the great majority of authorities.

To sum up, I would say that the paralysis of the laryngeal abductors in my patient was due to an infective neuritis of the laryn-

geal nerves, following an attack of influenza. In conclusion, may I say that after an extensive review of the bibliography this case seems to be the first of its kind reported in medical literature.

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14. Rebattu, M.: Les lésions anatomiques dans la paralysie des dilatateurs. Ann. d'Oto-Laryng., 4:381; (April) 1934.

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THE

ANNALS

OF

OTOLOGY, RHINOLOGY

AND

LARYNGOLOGY

CONTEMPLATES THE PUBLICATION

IN A SEPARATE VOLUME

OF AN

INDEX

OF ARTICLES

WHICH HAVE APPEARED IN

ITS PAGES FROM

1900 TO 1936

CROSS REFERENCES AND AUTHOR LISTINGS WILL BE ARRANGED WITH SPECIAL ATTENTION TO THE REQUIREMENTS OF STUDENTS, WRITERS AND INVESTIGATORS

Dan McKinzie

DAN McKENZIE.

Dan McKenzie, one of the best known and best loved British otolaryngologists, died in November. One has but to read the many tender messages from his colleagues which appeared in the British press to understand that McKenzie was not only an international figure in laryngology but a warm and sympathetic friend.

"His more intimate friends will remember," writes Mr. Herbert Tilley in the British Medical Journal, "that toward the end of last January, and two days after a major abdominal operation, he developed an acute and severe type of streptococcal laryngitis, which for a few days caused much distress to the patient and considerable anxiety to those in charge of him. Convalescence was slow, but some two months later he returned to work, though not without certain general symptoms, which made it evident that some degree of toxemia still persisted. As laryngologists, both the patient and I were very much interested in the local and general manifestations of a somewhat unusual and severe type of laryngeal infection, and for this reason we recorded and commented on his 'case' in the British Medical Journal of July 6th, 1935. It will be seen that under the heading "Symptomatology" the last paragraph reads: 'Finally, the slow convalescence may be further retarded by the onset of cardiac symptoms, due to the influence of the streptococcal toxins in the myocardium.' How little we imagined that this would be the ground on which the last battle would be fought—and lost!"

McKenzie began his professional life as a general practitioner among the mining population of Lanark, later serving his apprenticeship as a laryngologist in the Central London Throat, Nose and Ear Hospital. He was often a contributor to the programs of the Sections of Otology and Laryngology of the Royal Society of Medicine, over both of which he at some time presided. His writings were lucid and authoritative and at the same time revealed a charm which characterized the man. In a little volume called "Aromatics and the Soul" may be encountered as engaging an evening's reading as one is likely to find.

Chiefly from the Medical Directory the following list of McKenzie's affiliations and publications has been gathered:

McKENZIE, Dan, F.R.C.S. Ed. 1909; M.D. Glas. (commend.) 1898, M.B., C.M. (high commend.) 1891; (Univ. Glas.); Cheval. de la Legion d'Honn.; Chadwick Trust Lect. 1929; Hist. of Med. Prize, Univ. Glas. 1925; Cons. Surg. Centr. Lond. Throat & Ear Hosp.; Cons. Oto-Laryngol. French Hosp., Ealing & Chiswick, Wimbledon & Hendon Isolat. Hosps.; Fell. Roy. Soc. Med. (Ex-Pres. Laryng. & Otol. Sects.); Corr. Fell. Amer. Laryng. Assn.; Corr. Mem. Soc. franc. d'Oto-Laryngol.; Hon. Joint Sec. 17th Internat. Congr. Med. (Laryng. Sect.); late Regist. & Clin. Asst. Centr. Lond. Throat & Ear Hos.; Hon. Cons. Laryngol. Ilford Emerg. Hosp. Author, "Dis. of Throat, Nose and Ear." 2nd edit. 1927; "Diathermy in Otolaryngology," 1930; "Early Drainage of Mastoid Antrum in Acute Suppuration," Lancet, 1922; "Otosclerosis: A Clin. Analysis," J. Laryng. and Otol., 1932; "Osteomyelitis of the Skull," J. Laryng. and Otol., 1913, 1927; "The City of Din," 1916; "Aromatics and the Soul," 1923; "McMorro's Duck," 1925; "The Infancy of Medicine," 1927.

Books Received.

Recent Advances in Laryngology and Otology.

R. Scott Stevenson, M.D., Ch.B., F.R.C.S. (Edin.), Surgeon, Metropolitan Ear, Nose and Throat Hospital, etc., London. Cloth. Octavo, 346 pages with 128 illustrations, including 13 color plates. P. Blakiston, Son & Co., Philadelphia, 1935. Price $5.00.

This is an extremely comprehensive and useful review of progress in otology and laryngology. It is more satisfying and more practical than the annual reviews, in that the references fall within the last ten years, although frequent allusions are made to earlier works. This book is by no means another list of titles. The material is well selected, well digested, and, most important, is accurate in detail. This last should make the book especially valuable for teachers of advanced students.

Especially noteworthy are the unbiased presentations of such controversial subjects as the irradiation of tumors, the treatment of chronic sinusitis and of meningitis, vestibular function and otosclerosis.

This is not a textbook. It assumes a knowledge of the subject, and is therefore not recommended to students of general medicine. However, for house officers and graduate students preparing themselves for specialization or for qualification before an examining board—even for experienced otolaryngologists in search of precise information, this is the best that has come our way.

Otosclerosis.

Louis K. Guggenheim, M.D., F.A.C.S., Assistant Professor of Clinical Otolaryngology, Washington University School of Medicine. Cloth. Octavo, 212 pages with 127 illustrations. Privately printed and obtainable from Louis K. Guggenheim, 6227 Rosebury Ave., St. Louis. Price $6.00.

In a monograph of two hundred and twelve pages with one hundred and twenty original photomicrographs and thirty-five drawings of lower vertebrate ears, the author first reviews the various theories as to etiology and criticises these viewpoints. In the second chapter the theory of regression is explained, which regards the localized osseous dystrophy of the aural capsule as a throw-back to a lower vertebrate period in which the recently acquired labyrinthine windows and cochlea are nonexistent. The intimate relationship of the involvement at the site of predilection to the fissula ante fenestram is described in detail and well illustrated with numerous high magnification photomicrographs.

Other chapters deal with the evolution of the organ of equilibrium and hearing, from the lowest vertebrate (Myxine glutinosa) to man; the development of the ear in man, and the three stages of otosclerosis. The pathologic processes are followed, step by step, profusely illustrated with original photomicrographs. Of particular interest is the presentation for the first time of a six weeks' embryo from an otosclerotic mother. Autopsies of otosclerotic individuals are analyzed.

The work is an original contribution to a subject of the greatest importance to otologists. The subject matter is well arranged and clearly and simply expressed.

For Stutterers.

Smiley Blanton, M.D., Assistant Professor of Clinical Psychiatry, Cornell University Medical College, and Margaret Gray Blanton. Cloth. Octavo, 191 pages. New York: D. Appleton-Century Company. 1935. Price $2.00.

"Not primarily for parents or for teachers, although certain chapters have been addressed to them; nor for physicians, although if they find it suggestive we shall be grateful. But it is for those people with the symptom called stuttering, whom we feel to have been too long neglected."—*From the Author's Foreword.*

Diseases of the Nose and Throat.

Charles J. Imperatori, M.D., F.A.C.S., Professor of Clinical Otolaryngology, New York Post-Graduate Medical School, Columbia University, and Herman J. Burman, M.D., Instructor of Clinical Otolarynogology, New York Post-Graduate Medical School, Columbia University. Cloth. Octavo of 723 pages with 480 Illustrations. Philadelphia: J. B. Lippincott Company. 1935. Price $7.00.

Plastic Surgery and the Law (La chirurgie réparatrice dans ses rapports avec la jurisprudence).

C. Claoné and I. Bernard, Paris. Paper. 12mo of 30 pages. Maloine, Paris. 1935.

This article, reprinted from "L'Activités scientifique et médicale," was inspired by a heavy judgment against a Paris surgeon, and sets up the following desiderata for any plastic or cosmetic operation: 1. Consent of the patient or his family must be obtained; 2. The operation must have a curative object—be required by therapeutic necessity; 3. The operation must not be contrary to sound public policy—must not be purely experimental.

Claoné sets up a detailed estimate of operative, hospital and after-treatment expense, with a disclaimer clause stating that nothing in surgery can be guaranteed; he states that during seven years only two patients have refused to sign such a disclaimer.

The psychology of deformity and disfigurement is well discussed, and the dissatisfaction of patients with the best possible plastic results is pointed out. Commercialism, publicity and fee splitting in this field is condemned in the strongest terms. FENTON.

Chronic Laryngeal Tuberculosis in the Adult (La tuberculosis crónica de la laringe en el adulto).

G. Bonfill, Madrid. Paper. Octavo of 302 pages, illustrated. Cuesta, Madrid. 1935.

This manual, with its introduction by Professor Tapia, is fairly well documented in pathology, but its therapeutic recommendations follow the French and English school without reference to the authoritative work of Emil Mayer, Robert Levy, Dennis, Spencer and other American writers. It does not, therefore, fill an authoritative place in the annals of tuberculosis. FENTON.

Abscess of the Brain: Its Pathology, Diagnosis and Treatment.

E. Miles Atkinson, M.S., B.S., F.R.C.S. Cloth. Octavo, 280 pages with numerous illustrations. Medical Publications, Ltd., London, 1934.

Names of Surgical Operations.

Compiled and arranged by the Western Surgical Association. Edited by Carl E. Black, A.M., M.D., Jacksonville, Illinois. Cloth. Octavo of 102 pages. St. Paul, Bruce Publishing Company, 1935. Price $3.00.

Diathermy in Oto-Rhino-Laryngology (La Diathermie en Oto-Rhino-Laryngologie).

Joseph LeMoine, Assistant d'Oto-Rhino-Laryngologie de l'Hôpital Bretonneau with a preface by Dr. H. Bourgeois of the Hôpital Laënnec. Paper. Octavo, 392 pages with 235 illustrations. Second edition. Paris: Gaston Doin & Cie., 1935. 65 fr.

NOTICES.

THE AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.

The next annual meeting of the American Laryngological, Rhinological and Otological Society, Inc., will be held at the Brown Palace Hotel, Denver, Colo., May 18, 19 and 20, 1936.

C. STEWART NASH, M. D., Acting Secretary.

The Department of Otolaryngology of the Washington University School of Medicine will give a four weeks' graduate course in otolaryngology for otolaryngologists. This course will begin June 29, 1936.

Information may be had of the Registrar, Washington University School of Medicine, St. Louis, Mo.

Abstracts of Current Articles.

NOSE.

An Anatomical Investigation of Blood Vessels of the Lateral Nasal Wall and Their Relation to Turbinates and Sinuses.

Burnham, Howard H. (Toronto), J. Laryngol. and Otol., 50:569-593 (Aug.), 1935.

The author describes in detail the courses of blood vessels in the lateral wall of the nose, which have received only general descriptions in the textbooks. Numerous specimens were dissected, and two cadavers were specially injected with a fluid rubber solution and a Prussian blue gelatin mixture, respectively, for the detail work. Thirty-four hundred serial sections were made, and measurements from these were plotted on a photograph of the block.

In this way not only the pathways of the vessels but the bony grooves which accommodate them were accurately determined.

Experimental Researches of the Olfactory Sense, Attempting to Interpret Its Precise Mechanism (Ricerche sperimentali intorno al senso dell'olfatto, tendenti ad interpretare il meccanismo di percezione del medesimo).

Niccolini, P. (Firenze), Valsalva, 11:189-205 (April), 1935.

The author for the past four years has published articles on various phases of the olfactory apparatus and three more are in print.

In this paper he gives some conclusive facts of his previous work and acknowledges that, up to date, the function of the olfactory organ is not thoroughly understood.

He thinks that three factors combine in a perfect function of this apparatus.

The first is the odoriferous capacity of the various substances. He studies and discusses the olfactory properties of 210 elements and classifies them according to their ability of disseminating odors. He states that a substance to be odorous must possess a determined amount of volatility in the air and a certain solubility in the fluid which bathes the olfactory end organs. Therefore, the first requirement of the olfactory function depends on the physical (volatility and solubility) and on the chemical or chemicophysical nature of these substances.

The second depends on the composition of the nasal secretion and the chemical capacity of the mucous membrane. The author considers the ability of the nose of combining the oxygen molecule

in such a form to transfer to these substances the capability of becoming perceivable by the organ of smell.

On this theory Torrigiani has demonstrated the presence of oxygenation in the nasal secretion. The author has, microscopically, shown the presence of a large number of oxygenic granules in the epithelial and glandular cells; and from these cells the granules pass into the mucous secretion which covers them. This oxidation occurs alike in the olfactory and the respiratory mucosa.

He further states that sulphocyanic acid is a useful adjunct to the olfactory activity. He demonstrates first, that by stimulating the first cranial nerve (by the odoriferous substance) the concentration of the sulphocyanic acid increases, and second, a stimulation of the fifth nerve causes a decrease in the quantity of this acid.

The third factor of the triad is the oxygen. The oxygen must be present, either in the atmospheric air or in the blood, because if it would be eliminated certain substances could not be perceived by the olfactory apparatus. The author has not experimented on this phase of the subject.

SCIARRETTA.

Relation of Bronchiectasis to Infection of the Paranasal Sinuses.

Hodge, G. E. (Montreal), Arch. Otolaryng., 22:537 (Nov.), 1935.

The author summarizes that the association of nontuberculous bronchiectasis and infection of the paranasal sinuses is extremely common. Pulmonary collapse and pneumonitis, frequently noted in early childhood, so weaken the structure of the lungs that there is a suitable soil for subsequent infection. Bronchiectasis, as evidenced by the number of dry cavities reported in the lungs of both children and adults, is more frequent than was previously supposed. Infection of the sinuses associated with bronchiectasis may date from early childhood or may occur as a secondary infection in later life. The treatment of bronchiectasis is surgical. Any focus of infection should be, when possible, removed from the upper respiratory tract before surgical intervention on the lungs is attempted. Best results will be obtained from medical treatment if it is commenced in early childhood.

TOBEY.

PHARYNX

Chronic Tonsillitis in the Adult: A Clinical, Bacteriologic and Pathologic Study.

Hunnicutt, Jr., T. N., Sternstein, H. J., and McMahon, H. E. (Boston), Arch. Otolaryng., 22:744 (Dec.), 1935.

The authors summarize: Twenty-five consecutive cases in which a clinical diagnosis of chronic tonsillitis had been given were studied

from a clinical, bacteriologic and pathologic standpoint. It has been shown that from the clinical aspect a single or group of changes was not found in all the tonsils and that the clinical findings did not bear a constant relationship to the clinical history. From a bacteriologic standpoint, one type of flora was not observed constantly in the tonsils nor was any characteristic type of flora found showing a relationship either to the gross appearance of the tonsil or to the clinical signs and symptoms. From the standpoint of pathology the changes in the tonsil, though variable, were strikingly similar to those in a group of selected controls. The histologic changes, with the rare exception of the specific lesion of rheumatic fever, did not bear a definite relationship to the bacterial flora or to the clinical signs and symptoms.

TOBEY.

LARYNX

Contribution to the Diagnosis of Pulmonary Cancer. Role of Contrast Broncho-pneumography and of Bronchoscopy (Contribution au diagnostic du cancer pulmonaire. Role de la broncho-pneumographie contrastée et de la bronchoscopie).

Loza, M. Gonzalez, Bronchoscopie, Oesophagoscopie et Gastroscopie, 4:312 (Oct.), 1935.

The author reports eight cases of cancer of the lung and discusses the problem of diagnosis. Emphasizing the clinical polymorphism of the condition, he stresses the use of x-ray studies with contrast media which he has found very valuable, and of bronchoscopic examination which he has found indispensable. Since many pulmonary cancers become secondarily infected, they are easily confused with lung abscesses. He therefore advises that every lung abscess in a patient over forty-five years of age be suspected as a cancer until thorough study can rule out this possibility. He urges that every case of pulmonary suppuration have a diagnostic bronchoscopy, which may establish an early diagnosis of cancer. Since 55 per cent of all lung cancers in his statistics are endobronchial, a histologic diagnosis can be made by bronchoscopic biopsy in over half the cases.

KLAWANS.

Remarks on Cervico-Thoracic Emphysema Apropos Two Bronchial Foreign Bodies (Remarques sur l'emphysème cervico-thoracique apropos de deux corps étrangers des bronches.)

Soulas, A., Bronchoscopie, Oesophagoscopie et Gastroscopie, 4:338 (Oct.), 1935.

The author reports two cases in children of metallic, roughened bronchial foreign bodies, which had gone unrecognized for some time, and in which, following bronchoscopic manoeuvres, a sub-

cutaneous emphysema appeared, first in the neck and then extended over the chest and the abdomen. One child died of cervical and mediastinal cellulitis, the other recovered.

To explain this rare complication, the author suggests two hypotheses. Since this accident occurred with sharp, metallic foreign bodies which had been *in situ* for a long time, he thinks it probable that slow perforation of the bronchial wall had occurred, which was just short of completion at the time of intervention, or was complete but was plugged by the foreign body. The gentlest manipulation then would lead to perforation. However, since a perforation in a stem bronchus in the region of these foreign bodies is extrapleural and extrapulmonary, the air would have to travel a considerable distance through the fascial planes to appear subcutaneously in the neck without first invading the mediastinum.

Another possible explanation is that some minute tear may have been produced by the bronchoscopic manipulation in the region of the hypopharynx or the subglottic region from which a subcutaneous emphysema of the neck could be directly produced.

Since these cases occurred in expert hands, the author feels that earlier diagnosis and treatment of foreign bodies is most important in avoiding this complication, which might have a medico-legal angle.

KLAWANS.

Electro-coagulation for Malignant Tumors of the Larynx (Diathermo-coagulation pour tumeurs malignes du larynx.)

Eeman, F. G., Bronchoscopie, Oesophagoscopie et Gastroscopie, 4:346 (Oct.), 1935.

The author reports the successful prolonged palliation obtained by repeated electro-coagulation of the tumor through the direct laryngoscope in a case of laryngeal carcinoma which he considered improbable of cure by extensive, mutilating surgery. The treatment was ambulatory, simple and provoked little reaction, and the author recommends its more widespread use in these cases.

KLAWANS.

Cases of Lung Abscess Treated and Cured by Bronchoscopic Therapy (Quelques Cas d'Abcès du Poumon Traités et Guérés par la Bronchoscopo-Thérapie).

Rist, E., and Soulas, A., Bronchoscopie, Oesophagoscopie et Gastroscopie, 4:289 (Oct.), 1935.

The authors report twelve cases of lung abscess, eight acute abscesses (less than three months' duration) and four chronic cases,

with definite cures in every case following bronchoscopic therapy. They point out, however, that such cures are to be expected in about 70 per cent of acute cases, 50 per cent of cases of three to four months' duration, and only 20 per cent of older cases. On an average five or six treatments were necessary, although in one case eleven bronchoscopies were done. The treatment varies in detail with the case, but in general consists of cleaning out the main bronchi with sponges moistened with adrenalin, followed by instillation of gomenolated oil. They do not regard the general condition of the patient, however bad, as a contraindication to this therapy. Surgery is indicated when bronchoscopic treatment fails.

KLAWANS.

Very Serious Tracheo-Bronchial Obstruction Following Labor: Efficacy of Emergency Bronchial Aspiration (Très grave obstruction trachéo-bronchique survenue a la suite d'un accouchment. Efficacité de la broncho-aspiration d'urgence).

Soulas, A., Bronchoscopie, Oesophagoscopie et Gastroscopie, 4:351 (Oct.), 1935.

The author describes a case of severe asphyxia with cyanosis and retraction due to aspiration of vomitus following a normal delivery. This apparently moribund patient was quickly restored to normal by bronchoscopic aspiration of the trachea and bronchi done at the bedside without anesthesia.

KLAWANS.

A Very Severe Case of Postoperative Tracheobronchial Obstruction Successfully Treated by Emergency Bronchoscopic Aspiration (Un Cas Paticulièrement Grave d'Obstruction Trachéo-Bronchique Post-Opératoire. Traitment Efficace par lo Broncho-Opération d'Urgence.)

Monod, Robt., and Soulas, A., Bronchoscopie, Oesophagoscopie et Gastroscopie, 1:22 (Jan.), 1935.

The authors point out the importance of bronchoscopic aspiration as a pre- and post-operative measure as well as during surgical procedures for pulmonary suppuration. Due to various factors, such as the opening in the thoracic wall, interference with nerves, muscles, pain, pulmonary compression, inhibition of the cough reflex and anesthesia, which favor retention of suppurative materials with consequent obstruction, the postoperative period is especially dangerous.

They report a case of this type where severe asphyxia developed thirty-six hours after a thoracoplastic operation for lung abscess and was promptly and permanently relieved by bronchoscopic aspiration of retained pus.

KLAWANS.

EAR

Recent Advances in the Electro-physiology of Hearing.

Hallpike, C. S., London, J. Laryngol. and Otol., 50:672 (Sept.), 1935.

The author outlines his experiments with the Wever-Gray effect and describes his instrument by means of which continuous parallel records can be made of the electrical response to a sound through the ear and of the sound itself. Simultaneous oscillograms are shown from the base and the apex of the cochlea, showing the variation with frequency in the relative amplitude of the responses. The latent period of the cochlear response is shown to be approximately one ten-thousandth of one second.

Results of the degeneration of the cochlear fibers following the section of the eighth nerve are studied. The work confirms the accepted theory of tone localization in the cochlea, and attempts to throw some light upon the acceptability of the "telephone theory," which at present fails to satisfy the requirements for pitches above 2000 d.v.

The Origin of Hearing—Random Variation or Convergent Evolution? A Study of the Auditory Organ and Its Swim-bladder Connections in Fishes.

Evans, H. Muir (Lowestoft), J. Laryngol. and Otol., 50:649 (Sept.), 1935.

This is a critical and exhaustive (thirty-eight pages) review of hitherto scattered observations upon the hearing mechanisms of fishes and an attempt to find some underlying and unifying principle in the great diversity of structure of those organs. In each of the three families described, an anterior sac is in intimate relation with the auditory organ. This sac may act as a mydrophone; it may be double, in which case the posterior sac transmits vibrations to the anterior; it may be in immediate contact with the tympanic membrane and be attached to the sacculus.

It has been found that a central area at the base of the cerebellum connected with the acoustic tubercles varies in size with the habits of the fish, and the theory is advanced that fish have a greater power of audition than has been hitherto accepted.

Cerebellar Abscess (Les abcès du cervelet).

Ramadier, J., Caussé, R., Thomas, André, Barré, J. A., and Velter, E. (Report to the Eighth French Congress of Oto-neuro-ophthal., Nice, April, 1935. *Rev. d'Oto-neuro-ophthal.,* 13:1 (Jan.); 13:85 (Feb.); 13:727 (Dec.), 1935.

This monumental report includes a critical evaluation of the puncture methods of Cushing and Dandy, the dural incision of Eagleton, and the electrosurgical methods of Tobey, and will form an up-to-date reference handbook for diagnosis and treatment in this field.

In diagnosis, rigorously accurate vestibular studies are necessary, especially of spontaneous, usually horizontal nystagmus, and of past pointing. The Romberg test made with a plumb line attached to the head will pick up unsteadiness very readily. The patient's posture, method of walking, position in bed, should be carefully studied before forced routine postures are tested. Choking of the discs, unequal pupils or oculomotor pareses may be transitory and highly valuable as operative indications, as may also changes in nystagmus from horizontal to vertical, indicating extension toward the fourth ventricle.

The authors favor transoccipital exposure behind the sinus, pointing out the very small area accessible through the infected mastoid in front of the sinus, and the danger of subsequent hemorrhage involved in Eagleton's incision through the packed off sinus itself. They favor a two-stage operation, permitting meningeal walling off by iodine, unless Shambaugh's diathermy coagulation is used, when one anesthetic may be sufficient. Other operators have never reached the early successes of Macewen, doubtless because the latter had only large, well-limited abscesses of long duration, operated in two stages, used the burr rather than the mallet and chisel, and drained by a single large tube.

Cures nowadays run from 39 to 42 per cent for cerebral, only 12 to 25 per cent for cerebellar abscesses. Early and careful diagnostic study is imperative before localization can be undertaken. The complete report will repay careful reading.

FENTON.

Treatment of Acute Suppurative Otitis Media by Syringing With Alcohol.

Schmidt, Viggo (Copenhagen), J. Laryngol. and Otol., 50:594 (Aug.), 1935.

This author recommends a solution of 33 per cent alcohol with 2 per cent procain for washing ears in acute purulent otitis media. For 24 to 48 hours following incision of the drum membrane, sterile cotton pledgets and hot compresses are applied. After this, irrigation is carried out by means of a 10 or 20 cc. record syringe around the tapered nipple of which is pressed a perforated rubber disc 2½ cm. in diameter. The cone enters the outer part of the external meatus, and gentle pressure is used. This is repeated three or four times daily. It is claimed that the astringent action of the alcohol makes for improved drainage, both through the incision and the eustachian tube and introduces an antiseptic into the middle ear at a sufficiently early stage to anticipate serious involvement of the mastoid cavities.

There is little discomfort beyond that of having small amounts of the dilute spirit find its way into the nasopharynx.

Schmidt reports the following phenomenal observations: During an epidemic of scarlet fever in Copenhagen last winter there were 1,650 cases (!), 157 (9.5 per cent) of which developed acute suppurative otitis media. Forty-four and six-tenths per cent of these required mastoid operations. None had been syringed with alcohol. At another hospital of 1,107 patients, 139 (12.6 per cent) developed middle ear infections, all were syringed with alcohol and only 5.8 per cent required operation.

The Supposed Presence of Glands in the Mucosa of the Tympanic Cavity (Sulla supposta presenza di glandole nella mucosa della cassa timpanica).

Gioacchini, R. (Roma), Valsalva, 11:165-179 (March), 1935.

The article contains a detailed review of histologic investigations on the presence of the secreting glands in the tympanic mucosa; also seven photomicrographs of some serial sections of the middle ears obtained from children or fetuses.

The author reports his histologic studies and technic for preparing the specimen; the latter he considers important for an accurate and positive investigation, so that no alteration of the anatomic relations could occur.

He concludes that no glands, of any type, exist in the mucosa of the tympanic cavity. Affirmative reports have been recorded probably because the mucosa had been removed from the bone or because the mucosal invaginations had been mistaken for glands, as the glands were reported to exist only where these invaginations exist.

Further, he thinks that the presence of secreting glands would disturb the physiologic equilibrium of the tympanic cavity by the increase or decrease of their secretion, thus interfering with the hearing function.

SCIARRETTA.

A New Direction for the Treatment of Otosclerosis (Sobre hua nueva orientacion en el tratamiento de la otospengiosis).

Chiarino, A., and Alonso, J. M. (Montevideo), Ann. Oto-rino-lar., Uruguay, 5:2-81, 1935.

Considering parathyroid dysfunction with hypocalcemia as responsible for otosclerosis, these authors ligated the inferior thyroid artery in three cases with notable improvement in deafness and tinnitus; in three others not yet reported they have removed the left inferior parathyroid gland. Most of these cases have since operation shown an increased blood calcium.

FENTON.

Muskens' Theories of the Supravestibular System (Muskens: Le système supra-vestibulaire).

Hirsch, L. (Bordeaux), Rev. de L. O. R., 56:1234 (Dec.), 1935.

Muskens' recent book derives its great value from his demonstration that the supravestibular system of cerebral connections is really composed of six different systems. There are six forms of forced movements: in the frontal plane, to left and to right; in the horizontal plane, to left and to right; in the vertical plane, up and down. Each of these has its own route and its own central nuclei, and each has its own type of nystagmus. "Balancing" (horizontal plane), is associated with horizontal nystagmus; "rolling" (frontal plane), with rotatory nystagmus; "falling," forward or back (vertical plane), with vertical nystagmus. The slow component lateralizes to the side of the forced movement.

An excellent diagram of these connections and their nuclei, with an explanation of the associated lesions at various levels, clarifies this brief and interesting critique of Muskens' very scholarly work.

FENTON.

Evaluation of Caloric Tests in Localization of Lesions of the Posterior Fossa: A Study of Forty Verified Cases.

Maybaum, Jacob L., and Grossman, Morris (New York), Arch. Otolaryng., 22: 565 (Nov.), 1935.

The authors conclude that caloric tests are of definite value in the localization of a lesion of the posterior fossa. The differential diagnosis of an infratentorial from a supratentorial lesion can frequently be made. Cerebellar neoplasms which have invaded the surface of the cerebellum, because of pressure phenomena affecting the eighth nerve, may give signs of a neoplasm of the angle on otologic examination.

Caloric tests are of distinct value in the early diagnosis of a lesion of the cerebellopontile angle. The so-called characteristic finding in a case of neoplasm of the angle, namely, loss of reaction on testing of the opposite vertical canals, is frequently lacking. Other evidence of indirect pressure phenomena may be present on vestibular examination. A comparative diagnostic study by means of otologic, neurologic, surgical and postmortem observations on forty cases of lesions of the posterior fossa has been made.

An abstract of a discussion by Dr. Isidore Friesner of New York follows the paper.

TOBEY.

Contribution to the Study of the Absorbing Power of the Tympanic Membrane (Contributo allo studio del potere assorbente della membrana timpanica).

Gianni, O. (Parma), Valsalva, 11:157 (March), 1935.

The author in his experiments has avoided the use of drugs which are absorbed by the normal skin, such as nicotine, phenol, iodine, etc., but he used only crystalloids, such as atropin, pilocarpin, eserin, morphine, apomorphine, cocaine, etc., and also the colloidal preparations (adrenalin, etc.).

These medications were dissolved in a hyper-iso or hypotonic solutions of normal salt (NaCl), then from the results obtained he draws the following conclusions:

First he proves, by carefully excluding the tympanic membrane, that the tissue of the external auditory canal normally does not absorb any medication unless massage is applied or some inflammatory process exists.

Second, the tympanic membrane will absorb crystalloid drugs when they are dissolved in salt solution, but will not absorb the colloidals.

Finally, the absorption of the crystalloids in salt solution will take place rapidly if the solution is hypotonic, slower if isotonic and very slow if hypertonic, while if dissolved in plain sterile distilled water no absorption takes place.

Therefore, the tympanic membrane must be a semipermeable membrane which permits the crystalloid substances to be absorbed or pass through it only when they are suspended in a solution whose molecular concentration is similar to the blood serum of the subject in the experiment. SCIARRETTA.

MISCELLANEOUS

Wrong Diagnoses from the Laboratory (Fehldiagnosen des Laboratoriums.)

Prof. H. Burger (Amsterdam), Acta Oto-Lar., 23:2-207, 1935.

The wall of an inflamed cyst which worked through from the subglottic region to the skin in a woman of 72 was reported as tuberculous; biopsy of the dark red bilateral subglottic swelling also indicated tuberculosis. But routine blood examination was positive for syphilis, and the lesion disappeared with two weeks of antiluetic medication. Epithelioid pseudotubercles with necrotic centers, and regular giant cells, may thus be found in frankly luetic infections.

A second case of mastoidectomy with associated cervical adenitis in a boy of fifteen aroused excitement when a moderate postoperative temperature rise with slight chill was accompanied by almost total

loss of eosinophiles and lymphocytes with great increase in young forms of polymorphonuclears, 17,000 total W. B. C. Though advised to go into the jugular and remove the tonsils, Burger trusted the excellent clinical appearance of this patient, who recovered promptly. He warns against following laboratory findings unless they check accurately with the results of clinical observation.

FENTON.

Histologic Versus Clinical Evaluation of Upper Respiratory Epitheliomas (Des rapports de la maligorité histologique et clinique de l'épithelioma des voies aéro-digestives supérieures).

Portmann, G., Barraud, A., and Mougneau (Bordeaux), Rev. de L. O. R., 56: 926 (Sept.-Oct.), 1935.

Professor Portmann and his collaborators feel that histologic examination of epitheliomas does not furnish an accurate index either of radiosensitiveness or of the grade of malignancy; other factors are important, especially in the aged, where evolution of the growth from stage to stage may be very slow. One hundred cases, aged 65 to 82, were divided as follows: 26, nose or sinuses; 18, buccopharyngeal; 61, laryngeal. Biopsy, though essential, gives information which must be weighed against the clinical findings in mapping out treatment and prognosis. FENTON.

Sialography—Technique, Indications, Utility (La sialographie).

Fenz, J. (Lausanne), Rev. de L. O. R., 56:1037 (Nov.), 1935.

Detailing the submaxillary and vertex radiographic positions, the author shows that by injection of neoiodipin, more fluid than lipiodol, it is possible to map out calculi, cysts and abscesses of the submaxillary and parotid glands. Very small blunt probes and cannulas are used and 2 to 3 cc. of the oil is injected. Its therapeutic effect may be valuable during inflammation. Intrabuccal removal of calculi is recommended. Two plates are used for the parotid, shooting below the opposite horizontal ramus; both sides are taken from the vertex for the submaxillaries. FENTON.

NOTICE.

The summer postgraduate course in ophthalmology and otolaryngology at Denver, Colo., will be held from July 20 to August 1, 1936. The first week's study will be devoted to the eye, and the second week to the ear, nose and throat. The guest speakers will be Dr. Oscar V. Batson of Philadelphia, Dr. Lawrence T. Post of St. Louis, Dr. William L. Benedict of Rochester, Minn., and Dr. Will Otto Bell of Seattle. Inquiries regarding the course may be sent to Dr. H. L. Whitaker, 1234 Republic Building, Denver, Colo.